



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification<sup>6</sup> :C07D 239/54, 405/12, C07C 309/81,  
327/22, A01N 43/54

A1

(11) International Publication Number:

WO 98/28280

(43) International Publication Date:

2 July 1998 (02.07.98)

(21) International Application Number: PCT/US97/23546

(22) International Filing Date: 22 December 1997 (22.12.97)

(30) Priority Data:

60/033,835	23 December 1996 (23.12.96)	US
08/990,214	12 December 1997 (12.12.97)	US

(71) Applicant: FMC CORPORATION [US/US]; 1735 Market Street, Philadelphia, PA 19103 (US).

(72) Inventors: MARAVETZ, Lester, L.; 843 Carleton Road, Westfield, NJ 07090 (US). CRAWFORD, Scott, D.; 130 Birch Hollow Drive, Bordentown, NJ 08505 (US). THEODORIDIS, George; 45 Monroe Lane, Princeton, NJ 08540 (US).

(74) Agents: CALDWELL, John, W. et al.; Woodcock Washburn Kurtz Mackiewicz &amp; Norris LLP, 46th floor, One Liberty Place, Philadelphia, PA 19103 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

## Published

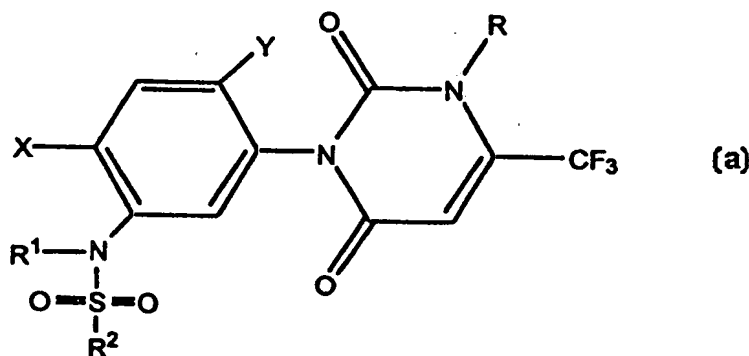
*With international search report.**Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.*

(54) Title: CERTAIN 3-[2,4-DISUBSTITUTED-5-(SUBSTITUTED AMINO)PHENYL]-1-SUBSTITUTED-6-TRIFLUOROMETHYL-2,4-(1H,3H)-PYRIMIDINEDIONE DERIVATIVES AS HERBICIDES

## (57) Abstract

Herbicidal compounds having structure (a) are disclosed, in which: X and Y are independently selected from hydrogen, halogen, and alkyl; R is alkyl or amino; R<sup>1</sup> is hydrogen, alkyl, cyanoalkylsulfonyl, acyl, acyloxyacyl, alkoxyacetyl, or represents the negative charge of the anion of a salt; R<sup>2</sup> is: (1) alkyl, cyanoalkyl, cyanoalkoxyacetylalkyl, alkenoxyacetylalkyl,

alkynoxyacetylalkyl, arylalkyl, aryloxyalkyl, arylalkoxyacetylalkyl, heterocyclyl, amino, aminocarbonylalkyl; (2) -W-R<sup>3</sup> in which W is alkyl, and R<sup>3</sup> is aminocarbonyl, alkoxyacetyl, hydroxyacetyl, arylalkylthiocarbonyl, nitro, alkylthiocarbonyl, or heterocyclylalkoxyacetyl; (3) -CH(C≡N)R<sup>4</sup> in which R<sup>4</sup> is hydrogen, alkyl, arylalkyl, or arylhaloalkyl; or (4) -C(C≡N)=CHR<sup>5</sup>; in which R<sup>5</sup> is aryl or heterocyclyl; with the proviso that an amino group may be substituted with alkyl, cyanoalkyl, alkoxy, alkoxyacetylalkyl, acyloxyacyl, aryl, arylalkyl, aryloxyalkyl, or heterocyclylalkyl; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with halogen; and heterocyclyl is selected from 2,3-dihydro-2,2-dimethylbenzofuran-7-yl and 1,3-dioxolan-2-yl. The sodium, potassium or 1-8 carbon amine salts of the compounds are also herbicidal.



(a)

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakhstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

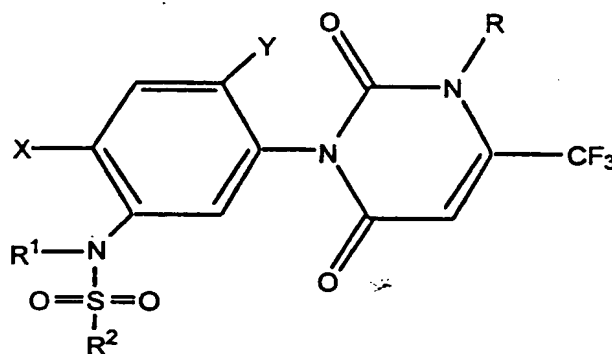
**CERTAIN 3-[2,4-DISUBSTITUTED-5-(SUBSTITUTED AMINO)PHENYL]-1-SUBSTITUTED-6-TRIFLUOROMETHYL-2,4-(1H,3H)-PYRIMIDINEDIONE DERIVATIVES AS HERBICIDES**

5

This invention relates to methods for controlling unwanted plant species in agriculture. In particular, it is the control by application of certain 3-[2,4-disubstituted-5-(substituted amino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1H,3H)-pyrimidinedione derivatives to a locus where herbicidal control is desired. While some 3-phenyl-1-substituted-6-trifluoromethyl-2,4-(1H,3H)-pyrimidinedione derivatives are known to have herbicidal activity, the use of the class of compounds of this invention as herbicides is heretofore unknown.

15

It has now been found that certain 3-[2,4-disubstituted-5-(substituted amino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1H,3H)-pyrimidinedione derivatives are highly active herbicides. The novel compounds of the present invention are defined by the following generic structure:



20

in which:

X and Y are independently selected from hydrogen, halogen, and alkyl;

R is alkyl or amino;

R<sup>1</sup> is hydrogen, alkyl, cyanoalkylsulfonyl, acyl, acyloxyacyl, alkoxycarbonyl,

25 or represents the negative charge of the anion of a salt;

R<sup>2</sup> is:

(1) alkyl, cyanoalkyl, cyanoalkoxycarbonylalkyl, alkenoxycarbonylalkyl, alkynoxycarbonylalkyl, arylalkyl, aryloxyalkyl, arylalkoxycarbonylalkyl, heterocyclyl, amino, aminocarbonylalkyl;

5 (2) —W—R<sup>3</sup> in which W is alkyl, and R<sup>3</sup> is aminocarbonyl, alkoxycarbonyl, hydroxycarbonyl, arylalkylthiocarbonyl, nitro, alkylthiocarbonyl, or heterocyclylalkoxycarbonyl;

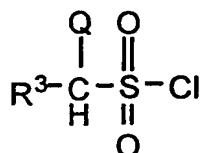
(3) —CH(C≡N)R<sup>4</sup>, in which R<sup>4</sup> is hydrogen, alkyl, arylalkyl, or arylhalo-alkyl; or

10 (4) —C(C≡N)=CHR<sup>5</sup>; in which R<sup>5</sup> is aryl or heterocyclyl;

with the proviso that an amino group may be substituted with one or two substituents independently selected from alkyl, cyanoalkyl, alkoxy, alkoxy-carbonylalkyl, acyloxyacyl, aryl, arylalkyl, aryloxyalkyl, and heterocyclylalkyl; halogen is chlorine, bromine, or fluorine; the alkyl and acyl moieties may  
15 each contain 1-6 carbon atoms, the alkenyl and alkynyl moieties may each contain 2-6 carbon atoms, each may be straight or branched, and the total number of carbon atoms in any R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, or R<sup>4</sup> does not exceed 12; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with halogen; and heterocyclyl is selected from 2,3-dihydro-2,2-dimethylbenzo-  
20 furan-7-yl and 1,3-dioxolan-2-yl;.

with the further proviso that when R<sup>2</sup> is amino, alkylamino, dialkylamino, arylamino, or arylalkylamino, and R is alkyl, R<sup>1</sup> is not hydrogen, alkyl, alkylcarbonyl, or alkoxycarbonyl; and

when R<sup>2</sup> is aryl arylalkyl, or alkoxycarbonylalkyl, and R is alkyl, R<sup>1</sup>  
25 cannot be hydrogen, alkyl, alkylcarbonyl, or alkoxycarbonyl, but R<sup>2</sup> may be alkyl only when R<sup>1</sup> is cyanoalkylsulfonyl or acyloxyacyl;  
or the sodium, potassium or 1-8 carbon amine salts thereof.



in which :

$\text{R}^3$  is selected from arylhaloalkyl, substituted or disubstituted amino-carbonyl, arylalkoxycarbonylalkyl, and (arylalkylthio)carbonyl; and

5 Q is hydrogen or alkyl;

with the proviso that the amino substituents are independently selected from alkyl, cyanoalkyl, alkoxy, alkoxycarbonylalkyl, aryl, arylalkyl, and aryloxyalkyl; the alkyl, alkoxy, and acyl moieties may each contain 1-6

10 carbon atoms in  $\text{R}^3$  does not exceed 12; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with chlorine, bromine, or fluorine.

Preferred are those compounds in which:

R is alkyl or amino;

$\text{R}^1$  is hydrogen, alkyl, acyl, acyloxyacyl, or represents the negative

15 charge of the anion of a salt;

$\text{R}^2$  is (1) cyanoalkyl, aryloxyalkyl, amino, or aminocarbonylalkyl, in which an amino group may be substituted with one or two substituents independently selected from alkyl, cyanoalkyl, or alkoxy; with the proviso that when  $\text{R}^2$  is amino, alkylamino, or dialkylamino, and R is alkyl,  $\text{R}^1$  is not

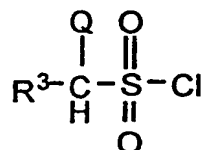
20 hydrogen or alkyl; or (2)  $-\text{CH}(\text{C}\equiv\text{N})\text{R}^4$ , in which  $\text{R}^4$  is hydrogen or alkyl; with the proviso that the alkyl, alkoxy, and acyl moieties may each contain 1-4 carbon atoms; each may be straight or branched; the total number of carbon atoms in any  $\text{R}^1$ ,  $\text{R}^2$ , or  $\text{R}^4$  is does not exceed 8; and aryl is selected from phenyl or furanyl.

25 Particularly preferred are those compounds in which X is chlorine or bromine; Y is hydrogen or fluorine; R is methyl or amino;  $\text{R}^1$  is hydrogen, acetyl, or acetoxycetyl;  $\text{R}^2$  is (1) 1-cyanoethyl, 2-cyanopropyl, phenoxyethyl, dimethylamino, (2-cyanoethyl)(methyl)amino, or aminocarboxymethyl, in

which an amino group may be substituted with one or two substituents independently selected from methyl, methoxy, phenyl, or benzyl; with the proviso that when  $R^2$  is dimethylamino, and  $R$  is methyl,  $R^1$  is not hydrogen; or (2)  $-\text{CH}(\text{C}\equiv\text{N})\text{R}^4$ , in which  $R^4$  is hydrogen or alkyl.

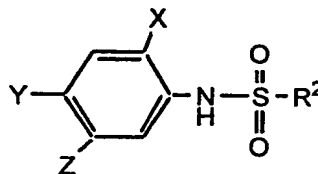
- 5 Novel intermediates useful in the preparation of the compounds of this invention include the following :

(1)



- in which:  $R^3$  is selected from arylhaloalkyl, substituted or disubstituted aminocarbonyl, arylalkoxycarbonylalkyl, and (arylalkylthio)carbonyl; and Q is hydrogen or alkyl; with the proviso that the amino substituents are independently selected from alkyl, cyanoalkyl, alkoxy, alkoxycarbonylalkyl, aryl, aryllkyl, and arylxyalkyl; the alkyl, alkoxy, and acyl moieties may each contain 1-6 carbon atoms, each may be straight or branched, and the total number of carbon atoms in  $R^3$  does not exceed 12; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with chlorine, bromine, or fluorine;

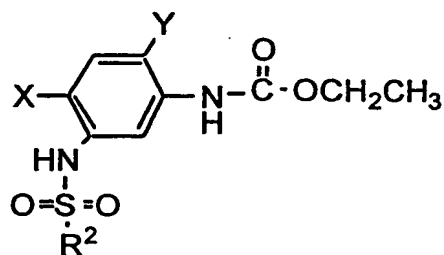
(2)



- in which: X and Y are independently selected from hydrogen, halogen, and alkyl; Z is nitro, amino, or isocyanato;  $R^2$  is arylalkyl, aryloxyalkyl, cyanoalkyl, substituted or disubstituted aminocarbonylalkyl, arylalkoxycarbonyl-alkyl, (arylalkylthio)carbonylalkyl, or mono- or disubstituted amino; with the proviso that the amino substituents are independently selected from alkyl, cyanoalkyl, alkoxy, alkoxycarbonylalkyl,

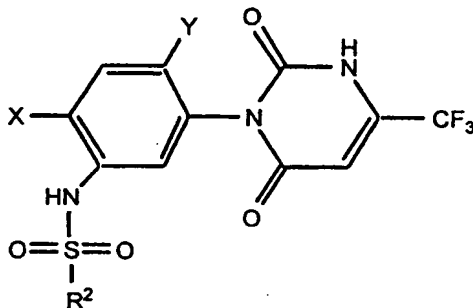
acyloxyacyl, aryl, arylalkyl, and aryloxyalkyl; the alkyl, alkoxy, and acyl moieties may each contain 1-6 carbon atoms, each may be straight or branched, and the total number of carbon atoms in  $R^2$  does not exceed 12; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with chlorine, bromine, or fluorine;

(3)



in which: X and Y are independently selected from hydrogen, halogen and alkyl;  $R^2$  is arylalkyl, aryloxyalkyl, cyanoalkyl, substituted or disubstituted aminocarbonylalkyl, arylalkoxycarbonylalkyl, (arylalkylthio)carbonylalkyl, or disubstituted amino; with the proviso that the amino substituents are independently selected from alkyl, cyanoalkyl, alkoxy, alkoxycarbonylalkyl, acyloxyacyl, aryl, arylalkyl, and aryloxyalkyl; the alkyl, alkoxy, and acyl moieties may each contain 1-6 carbon atoms, each may be straight or branched, and the total number of carbon atoms in  $R^2$  is does not exceed 12; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with chlorine, bromine, or fluorine; and

(4)



in which: X and Y are independently selected from hydrogen, halogen, or alkyl; and R<sup>2</sup> is arylalkyl, aryloxyalkyl, cyanoalkyl, substituted or disubstituted aminocarbonylalkyl, arylalkoxycarbonylalkyl, (arylalkylthio)-carbonyl-alkyl, or mono- or disubstituted amino; with the proviso that the amino substituents are independently selected from alkyl, cyanoalkyl, alkoxy, alkoxycarbonylalkyl, acyloxyacyl, aryl, arylalkyl, and aryloxyalkyl; the alkyl, alkoxy, and acyl moieties may each contain 1-6 carbon atoms, each may be straight or branched, and the total number of carbon atoms in R<sup>2</sup> does not exceed 12; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with chlorine, bromine, or fluorine.

The compounds of the present invention were prepared by methods known to one skilled in the art. A number of synthesis routes were employed in obtaining the targeted compounds.

Generally, the 3-[2,4-disubstituted-5-(substituted amino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione compounds were prepared by one of two routes, depending on whether the substitution at the five position of the phenyl ring occurs prior to, or after, the formation of 2,4-(1*H*,3*H*)-pyrimidinedione ring.

As depicted in Schema 1, compounds in which the substitution at the five position of the phenyl ring occurs after the formation of the 2,4-(1*H*,3*H*)-pyrimidinedione ring are prepared by reacting the appropriate 3-(2,4-disubstituted-5-aminophenyl)-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione (AA) with a substituted sulfonyl chloride (BB) in essentially equimolar-molar proportions to form the targeted 3-[2,4-disubstituted-5-(substituted sulfonylamino)phenyl]-1-(substituted or unsubstituted)-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione (I), for example 3-[4-chloro-2-fluoro-5-(2,3-dihydro-2,2-dimethylbenzofuran-7-ylsulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione. The reaction is facilitated by the use of solvents such as hydrocarbons, methylene chloride, chloroform, toluene, acetonitrile, diethyl ether, dioxane, pyridine,

tetrahydrofuran, and by the addition of bases, such as triethylamine or pyridine. These bases act as hydrogen chloride scavengers for the hydrogen chloride by-product of these reactions. Examples 4, 7, 8, and 9 provide detailed procedures for this route.

5        In other cases, the above reaction may be run in the prescribed solvents, such as acetonitrile, with two equivalents of the pyrimidinedione (AA) and one equivalent of the sulfonyl chloride (BB), which allows the pyrimidinedione (AA) to serve as the hydrogen chloride scavenger. Examples 1, 3, and 5 provide detailed procedures for this route.

10      In still other cases, particularly where the reactivity of the sulfonyl chloride (BB) is relatively low, the pyrimidinedione (AA) can be reacted in a large stoichiometric excess of the sulfonyl chloride (BB), without the use of a solvent and with a base such as 4-dimethylaminopyridine (DMAP). Example 13 provides a detailed procedure for this route.

15        Certain 3-[2,4-disubstituted-5-(substituted sulfonylamino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione (I), where R<sup>2</sup> is cyanomethyl, are susceptible to reaction with certain aryl or heterocyclic aldehydes, such as benzaldehyde or furfuraldehyde, under base-catalyzed dehydration, affording the targeted 3-[2,4-disubstituted-5-

20      (arylethenesulfonylamino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione (II). Example 2 provides a detailed procedure for this route.

Certain 3-[2,4-disubstituted-5-(substituted sulfonylamino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione (I) or (II) are also subject to salt formation by reaction of the sulfonamido group with bases,

25      such as sodium methoxide, sodium hydroxide, potassium hydroxide, potassium carbonate, or with organic alkylamines, such as isopropylamine, in a suitable solvent system. Example 6 provides a detailed procedure for this route.

The aminating agent can be prepared at this point. For example,

30      2,4,6-trimethylbenzene-sulfonyl chloride is reacted with *t*-butyl N-

hydroxycarbamate under basic conditions to yield *t*-butyl N-(2,4,6-trimethylphenylsulfonyloxy)carbamate (**CC**). The *t*-butyl carbamate (**CC**) is hydrolyzed under basic conditions, yielding 1-aminooxysulfonyl-2,4,6-trimethylbenzene (**DD**). Other aminating agents that could have utility  
5 include, but are not limited to, 2,4-dinitrophenoxyamine and hydroxylamine-O-sulfonic acid. The 1-aminooxysulfonyl-2,4,6-trimethylbenzene (**DD**) aminating agent is then reacted with the appropriate 3-[2,4-disubstituted-5-(substituted sulfonylamino)phenyl]-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione (**I**) where R is hydrogen, under basic conditions, affording  
10 the targeted 3-[2,4-disubstituted-5-(substituted sulfonylamino)phenyl]-1-amino-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione (**III**). Examples 10, 11 and 14 provide detailed procedures for this route.

The 3-[2,4-disubstituted-5-(substituted sulfonylamino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione (**I**) can be alkylated  
15 or acylated at the nitrogen atom of the sulfonamido group with such reagents as alkyl halides, acyl halides, acyloxyacyl halides, alkoxycarbonyl halides, with suitable solvents, such as methylene chloride, tetrahydrofuran, toluene, and diethyl ether, as well as bases, such as triethylamine or pyridine. Example 12 provides a detailed procedure for this route.

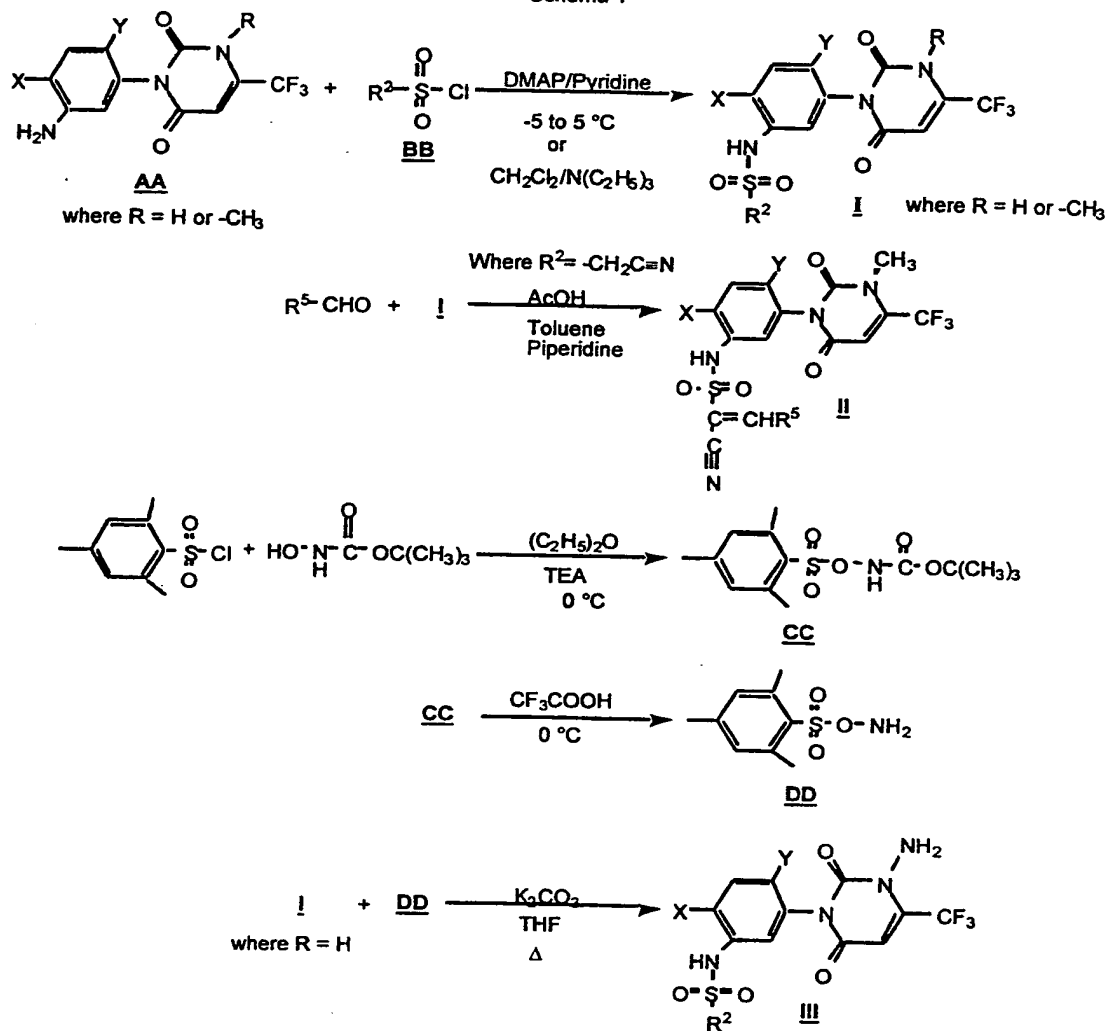
20 As depicted in Schema 2, those compounds in which the substitution at the five position of the phenyl ring occurs prior to the formation of 2,4-(1*H*,3*H*)-pyrimidinedione ring were prepared by reacting a substituted 5-aminophenylcarbamate ester (**EE**) with a sulfonyl chloride (**BB**) in the manner described previously to yield the corresponding ethyl N-[substituted 5-  
25 (substituted sulfonylamino)phenyl]carbamate (**FF**). At this point additional substituents may be added to the ethyl N-[substituted 5-(substituted sulfonylamino)phenyl]carbamate (**FF**). For example, the carbamate (**FF**) can be chlorinated by exposing it to an excess of chlorine gas in the presence of acetic acid and water, affording the ethyl N-[4-chloro-5-(substituted  
30 sulfonylamino)phenyl]carbamate. The carbamate (**FF**) is then reacted with

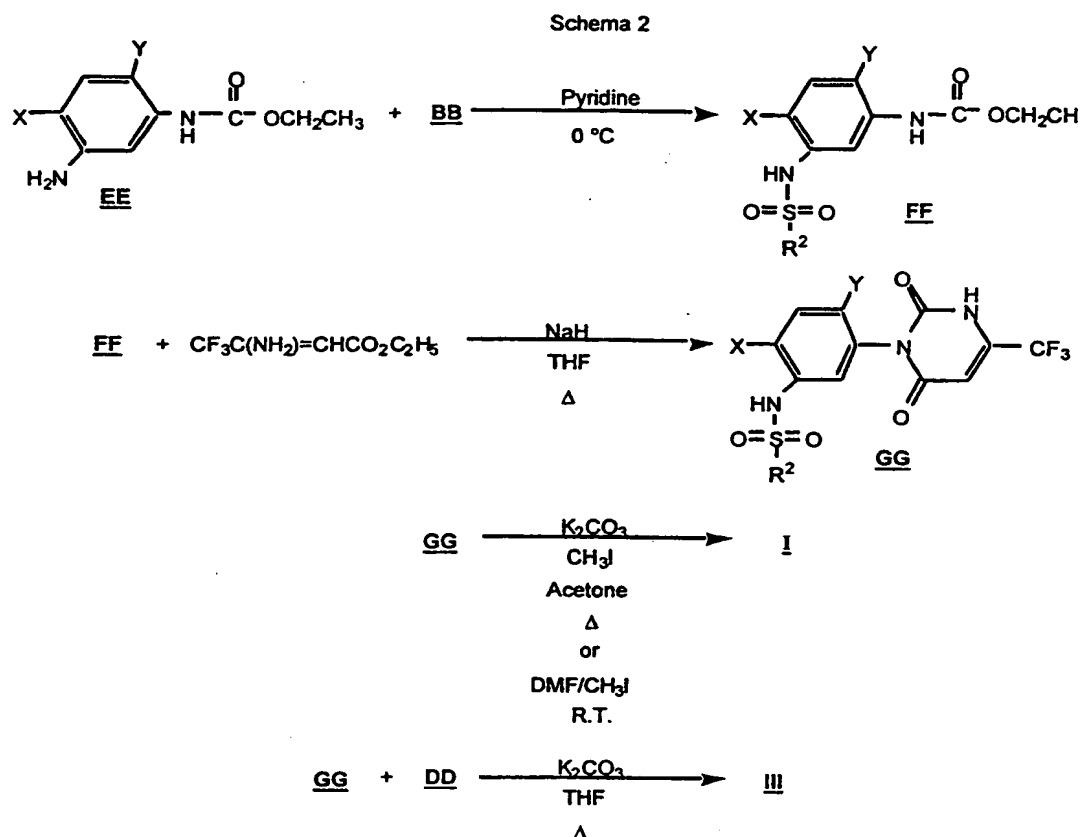
ethyl 3-amino-4,4,4-trifluorocrotonate in the presence of a base, such as sodium hydride, sodium methoxide, or alkaline earth metals, such as barium hydroxide, barium oxide, calcium hydroxide, calcium hydride, or strontium oxide, and then worked up with acid to form the corresponding 3-[2,4-disubstituted-5-[(alkylamino or aryl)sulfonylamino]phenyl]-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione (GG). The pyrimidinedione (GG) is in turn alkylated with methyl iodide or aminated with an aminating agent, for example, 1-aminooxysulfonyl-2,4,6-trimethylbenzene (DD), in the manner disclosed previously, affording the targeted 3-[2,4-disubstituted-5-(substituted sulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione (I) or 3-[2,4-disubstituted-5-(substituted sulfonylamino)phenyl]-1-amino-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione (III), respectively. Example 11 describes a detailed procedure for this route. Examples 10 and 14 also describe detailed procedures for this route, although with some variations that are known to those skilled in the art.

The substituted sulfonyl chlorides (BB) used to prepare the appropriate 5-sulfonamidophenyl derivatives of the present invention may be prepared by methods taught in the literature and known to those skilled in the art. Thus, a chloroacetamide can be converted to a sodium sulfonate with sodium sulfite in the presence of water and ethanol, followed by conversion to the sulfonyl chloride via phosphorous oxychloride in toluene. Example 9 describes a detailed procedure for preparing a substituted sulfonyl chloride (BB) by this route. Examples 7 and 8 describe similar reactions to yield other substituted sulfonyl chlorides (BB).

Similarly, a substituted dialkylaminosulfonyl chloride derivative (BB) can be prepared by reacting a secondary amine with sulfuryl chloride in chloroform. Example 13 describes a detailed procedure for preparing a sulfonyl chloride (BB) by this route.

Schema 1





## EXAMPLE 1

5      SYNTHESIS OF 3-[4-CHLORO-5-(CYANOMETHYLSULFONYLAMINO)-  
 PHENYL]-1-METHYL-6-TRIFLUOROMETHYL-2,4(1*H*,3*H*)-  
 PYRIMIDINEDIONE (COMPOUND 63)

A stirred solution of 1.0 gram (0.003 mole) of 3-(5-amino-4-chloro-  
 10      phenyl)-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione in about 13  
 mL of acetonitrile was cooled to -10 to 0 °C, and a solution of 0.2 gram  
 (0.002 mole) of cyanomethylsulfonyl chloride in 3 mL of acetonitrile was  
 added slowly. Upon completion of the addition the reaction mixture was  
 allowed to warm to ambient temperature, where it stirred for about three  
 15      hours. After this time the reaction mixture was concentrated under reduced  
 pressure, yielding 1.1 grams of a tan solid, which was taken up in about 20

mL of chloroform. The remaining solid was collected by filtration, yielding 0.1 gram of a gray solid. After an additional amount of chloroform was added to bring the total volume to about 20-25 mL, the above filtrate was re-filtered. The filter cake was dried, yielding 0.2 gram of 3-[4-chloro-5-

5 (cyanomethylsulfonylamino)-phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione, m.p. 220-223° C. The NMR spectrum was consistent with the proposed structure. The filtrate from the second filtering was concentrated under reduced pressure, yielding 0.8 gram of a solid. This solid was combined with the 0.1 gram of the above gray solid to yield a total of 0.9

10 gram of solid. The combined solid was taken up in a minimal amount of acetone, and the resulting solution was subjected to column chromatography on silica gel. Elution was accomplished with 1:1 ethyl acetate and hexane followed by pure ethyl acetate as eluants. The product-containing fractions were combined and concentrated under reduced pressure, yielding 0.4 gram

15 of 3-[4-chloro-5-(cyanomethylsulfonylamino)-phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione. The NMR spectrum was consistent with the proposed structure. This 0.4 gram of product was combined with the previous 0.2 gram of product to yield a total of 0.6 gram of 3-[4-chloro-5-(cyanomethylsulfonylamino)-phenyl]-1-methyl-6-trifluoromethyl-

20 2,4(1*H*,3*H*)-pyrimidinedione.

## EXAMPLE 2

### 25 SYNTHESIS OF 3-[4-CHLORO-5-(1-CYANO-2-PHENYLETHENE-SULFONYLAMINO)PHENYL]-1-METHYL-6-TRIFLUOROMETHYL-2,4(1*H*,3*H*)-PYRIMIDINEDIONE (COMPOUND 83)

A stirred solution of 0.4 gram (0.0009 mole) of 3-[4-chloro-5-(cyano-

methysulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-

pyrimidinedione (as prepared in Example 1), 0.1 gram (0.0009 mole) of

30 benzaldehyde, about 0.01 gram (0.0002 mole) of acetic acid, and 2-3 drops of piperidine in 15 mL of toluene was heated at reflux for two hours in the

presence of 3Å molecular sieves. At the conclusion of this period the reaction mixture was analyzed by TLC, which indicated that no starting material remained. The reaction mixture was decanted from the molecular sieves, diluted with more toluene, and then washed with one portion of 2N aqueous hydrochloric acid, followed by water. The resulting precipitate was collected by filtration, yielding 0.14 gram of 3-[4-chloro-5-(1-cyano-2-phenylethenesulfonylamino)-phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione, m.p. 241-243° C. The NMR spectrum was consistent with the proposed structure. The filtrate was washed with water, dried with magnesium sulfate, and re-filtered. This filtrate was concentrated under reduced pressure, yielding a moist solid. The toluene in the solid was extracted with two portions of petroleum ether to yield an additional 0.13 gram of 3-[4-chloro-5-(1-cyano-2-phenylethenesulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione. The NMR spectrum was consistent with the proposed structure. This 0.13 gram of product was combined with the 0.14 gram of product isolated previously to yield a total of 0.27 gram of 3-[4-chloro-5-(1-cyano-2-phenylethenesulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione.

20

## EXAMPLE 3

SYNTHESIS OF 3-[4-CHLORO-2-FLUORO-5-(1-CYANOETHYL-SULFONYLAMINO)PHENYL]-1-METHYL-6-TRIFLUOROMETHYL-2,4(1*H*,3*H*)-PYRIMIDINEDIONE (COMPOUND 68)

25

This compound was prepared in the manner of Example 1, with 0.7 gram (0.002 mole) of 3-(5-amino-4-chloro-2-fluorophenyl)-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione and 0.2 gram (0.001 mole) of 1-cyanoethylsulfonyl chloride in 10.0 mL of acetonitrile as reagents. The yield of 3-[4-chloro-2-fluoro-5-(1-cyanoethylsulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione was 0.2 gram, m.p. 107-110° C. The NMR spectrum was consistent with the proposed structure.

30

## EXAMPLE 4

5 SYNTHESIS OF 3-[4-CHLORO-2-FLUORO-5-(2,3-DIHYDRO-2,2-DIMETHYLBENZOFURAN-7-YLSULFONYLAMINO)PHENYL]-1-METHYL-6-TRIFLUOROMETHYL-2,4(1*H*,3*H*)-PYRIMIDINEDIONE (COMPOUND 1)

A stirred solution of 0.5 gram (0.001 mole) of the 3-(5-amino-4-chloro-2-fluorophenyl)-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione and 0.04 gram (0.0003 mole) of 4-dimethylaminopyridine in about 3 mL of  
10 pyridine was cooled to -5 to 5° C, and 0.4 gram (0.002 mole) of 2,3-dihydro-2,2-dimethylbenzofuran-7-ylsulfonyl chloride was added in small portions during a ten minute period. Upon completion of the addition the reaction mixture was allowed to warm to ambient temperature,, where it stirred for one hour. After this time the reaction mixture was analyzed by TLC, which  
15 indicated the reaction was complete. The reaction mixture was quenched with about 60 mL of aqueous 10% hydrochloric acid, and the resulting solid was collected by filtration. The solid was washed with water and dried on a clay plate to yield 0.7 gram of material, which was recrystallized from diethyl ether and water, yielding 0.3 grams of 3-[4-chloro-2-fluoro-5-(2,3-dihydro-2,2-  
20 dimethylbenzofuran-7-ylsulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione, m.p. 202-204° C. The NMR spectrum was consistent with the proposed structure.

## EXAMPLE 5

SYNTHESIS OF 3-[4-CHLORO-2-FLUORO-5-(1-CYANOPROPYL-SULFONYLAMINO)PHENYL]-1-METHYL-6-TRIFLUOROMETHYL-2,4(1*H*,3*H*)-PYRIMIDINEDIONE (COMPOUND 71)

5

This compound was prepared in the manner of Example 1, with 1.0 gram (0.003 mole) of 3-(5-amino-4-chloro-2-fluorophenyl)-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione and 0.2 gram (0.001 mole) of 1-cyanopropylsulfonyl chloride in 18 mL of acetonitrile as reagents. The yield of 3-[4-chloro-2-fluoro-5-(1-cyanopropylsulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione was 0.2 gram, m.p. 94-98° C. The NMR spectrum was consistent with the proposed structure.

10

## EXAMPLE 6

15 SYNTHESIS OF THE SODIUM SALT OF 3-[4-CHLORO-2-FLUORO-5-(1-CYANOETHYLSULFONYLAMINO)PHENYL]-1-METHYL-6-TRIFLUOROMETHYL-2,4(1*H*,3*H*)-PYRIMIDINEDIONE (COMPOUND 80)

A stirred solution of 1.2 grams (0.003 mole) of 3-[4-chloro-2-fluoro-5-(1-cyanoethylsulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione (as prepared in Example 3) and 0.1 gram (0.003 mole) of sodium methoxide in 25 mL of absolute methanol was heated to 40° C, where it stirred for five minutes. At the end of this period the reaction mixture was allowed to cool to ambient temperature during a 45 minute period, after which the absolute methanol was removed, yielding 1.3 grams of a tan solid. The solid was triturated with about 20 mL of diethyl ether, and the resulting supernatant liquid was decanted. To the remaining precipitate was added an additional 20 mL of diethyl ether, and again the supernatant liquid was decanted. The residual solid was dried, yielding 0.6 gram of the sodium salt of 3-[4-chloro-2-fluoro-5-(1-cyanoethylsulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione. The NMR spectrum was consistent with the proposed structure. The diethyl ether supernatant liquids

20

25

30

were combined and concentrated under reduced pressure, yielding an additional 0.7 gram of the sodium salt of 3-[4-chloro-2-fluoro-5-(1-cyanoethylsulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione.

5

## EXAMPLE 7

SYNTHESIS OF 3-[4-CHLORO-2-FLUORO-5-[(2-CHLORO-2-PHENYL-1-CYANO)ETHYLSULFONYLAMINO]PHENYL]-1-METHYL-6-TRIFLUOROMETHYL-2,4(1*H*,3*H*)-PYRIMIDINEDIONE (COMPOUND 77)

10

Step A            Synthesis of sodium 2-phenyl-1-cyanoethylsulfonate and sodium chloride mixture as an intermediate

To a stirred slurry of 4.2 grams (0.033 mole) sodium sulfite in 15 mL of water was added 4.2 grams (0.025 mole) of 1-chloro-2-phenylpropionitrile during a 30 minute period. Upon completion of the addition the reaction mixture was stirred at ambient temperature for one hour. After this time the reaction mixture was heated to 85° C, where it stirred for about 18 hours and then to 98-103° C, where it stirred for 1.5 hours. At the conclusion of this period the water was removed under reduced pressure, yielding a white residue, which was air dried, yielding 8.1 grams of organic product and sodium chloride. The NMR spectrum indicated the organic product to be sodium 2-phenyl-1-cyanoethylsulfonate. The material was used as is in the next step.

25    Step B            Synthesis of 2-chloro-2-phenyl-1-cyanoethylsulfonyl chloride as an intermediate

To stirred phosphorus oxychloride, 41.1 grams (0.27 moles), was added in portions 8.0 grams (0.01mole) of the sodium 2-phenyl-1-cyanoethylsulfonate and sodium chloride mixture during a five minute period followed by 15.0 grams (0.07 mole) of phosphorus pentachloride during a ten minute period. Upon completion of the addition the reaction mixture was

30

heated at 66-81° C for three hours, the cooled to ambient temperature and filtered. The filtrate was concentrated under reduced pressure, yielding 3.0 grams of crude product. This crude product was combined with 4.0 grams of crude product prepared by a similar route to yield a total of 7.0 grams of crude product, which were purified by distillation, yielding 2.4 grams of 2-chloro-2-phenyl-1-cyanoethylsulfonyl chloride. The IR spectrum was consistent with the proposed structure.

Step C      Synthesis of 3-[4-chloro-2-fluoro-5-[(2-chloro-2-phenyl-1-cyano)-ethylsulfonylamino]phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione (Compound 77)

A stirred solution of 0.5 gram (0.002 mole) of 3-(5-amino-4-chloro-2-fluorophenyl)-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione and 0.2 gram (0.002 mole) of triethylamine in 10 mL of tetrahydrofuran was cooled to 0° C, and a solution of 0.4 gram (0.002 mole) of 2-chloro-2-phenyl-1-cyanoethylsulfonyl chloride in 5 mL of tetrahydrofuran was added dropwise. Upon completion of the addition, the reaction mixture was allowed to warm to ambient temperature, where it stirred for one hour. After this time the reaction mixture was analyzed by TLC, which indicated that some starting material remained. The reaction mixture was again cooled to 0° C, and an additional 0.2 gram (0.002 mole) of triethylamine and 0.4 gram (0.002 mole) of 2-chloro-2-phenyl-1-cyanoethylsulfonyl chloride were added. Upon completion of this addition the reaction mixture was again allowed to warm to ambient temperature, where it stirred for about 18 hours. At the conclusion of this period the reaction mixture was again analyzed by TLC, which indicated that most of the starting material had reacted. The reaction mixture was filtered, and the filtrate was concentrated under reduced pressure to a brown oil, which was subjected to column chromatography on silica gel. Elution was accomplished with 2:5 methanol and methylene chloride followed by 1:1 ethyl acetate and hexane as eluants. The product-containing fractions were combined and concentrated under reduced pressure, yielding 0.1 gram

of 3-[4-chloro-2-fluoro-5-[(2-chloro-2-phenyl-1-cyano)ethylsulfonylamino]phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione, m.p. 188-190° C. The NMR spectrum was consistent with the proposed structure.

5

## EXAMPLE 8

SYNTHESIS OF 3-[4-CHLORO-2-FLUORO-5-[(1-BENZYLTHIO-CARBONYL)ETHYLSULFONYLAMINO]PHENYL]-1-METHYL-6-TRIFLUOROMETHYL-2,4(1*H*,3*H*)-PYRIMIDINEDIONE (COMPOUND 53)

10    Step A        Synthesis of 1-benzylthiocarbonyl-1-bromoethane as an intermediate

To a stirred solution of 7.6 grams (0.05 mole) of triethylamine in 100 mL of chloroform was added 5.3 mL of benzyl mercaptan in one portion.

15    Upon completion of the addition the mixture was stirred for ten minutes, and then a solution of 5.0 mL (0.04 mole) of 2-bromopropionyl chloride in 100 mL of chloroform was added dropwise. The reaction mixture was stirred for about 18 hours, then poured into 50 mL of an aqueous saturated sodium chloride solution and washed with water. The resulting mixture was poured  
20    into water and washed with one 50 mL portion of water followed by one 50 mL portion of aqueous 2N hydrochloric acid. The organic layer was separated from the aqueous layer, dried with magnesium sulfate, and filtered. The filtrate was concentrated under reduced pressure, yielding 12.8 grams of 1-benzylthiocarbonyl-1-bromoethane. The NMR spectrum was consistent  
25    with the proposed structure.

Step B        Synthesis of sodium 1-(benzylthiocarbonyl)ethylsulfonate and sodium bromide mixture as an intermediate

A stirred mixture of 2.4 grams (0.02 mole) sodium sulfite, 5.0 grams  
30    (0.02 mole) of 1-benzylthiocarbonyl-1-bromoethane [I], 10 mL of water, and 5 mL of ethanol was heated to 80° C during a two hour period. At the conclusion of this period the reaction mixture was analyzed by TLC, which indicated that some starting material remained. An additional 5 mL of

ethanol was added, and the reaction mixture was stirred at 80° C for an additional 45 minutes. After this time the reaction mixture was analyzed by NMR, which indicated the reaction was incomplete. An additional 25 mL of ethanol and 15 mL of water were added and the reaction mixture was stirred at 80° C for about 72 hours. The reaction mixture was again analyzed by TLC, which again indicated that some of the starting material remained. The reaction mixture was allowed to cool to ambient temperature, where it stood for 22 days. At the conclusion of this period, the water and ethanol were removed, yielding about 8.9 grams of a moist white solid, which was taken up in 100 mL of water. The resulting mixture was heated to 90° C, where it stirred for about 18 hours. After this time the heat was removed, and additional water was added. The mixture was extracted with two portions of methylene chloride. The combined methylene chloride extracts were dried with magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure, yielding 1.4 grams of total product. The NMR spectrum was consistent with the proposed structure. The aqueous phase from the above extraction was concentrated under reduced pressure, dried under vacuum at 40° C for three hours, yielding 4.8 grams of sodium 1-(benzylthiocarbonyl)ethylsulfonate. The NMR spectrum was consistent with the proposed structure.

Step C          Synthesis of 1-(benzylthiocarbonyl)ethylsulfonyl chloride as an intermediate

This compound was prepared in the manner of Step B, Example 7, with 8.0 mL (0.09 mole) of phosphorus oxychloride, 4.8 grams (0.02 mole) of sodium 1-(benzylthiocarbonyl)ethylsulfonate, and 50 mL of toluene as reagents. This preparation differed in that toluene was used in place of phosphorus pentachloride. The yield of 1-(benzylthiocarbonyl)ethylsulfonyl chloride was 2.8 grams. The NMR spectrum was consistent with the proposed structure.

5           Step D           Synthesis of 3-[4-chloro-2-fluoro-5-[(1-benzylthiocarbonyl)-ethylsulfonylamino]phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione (Compound 53)

10           This compound was prepared in the manner of Step C, Example 7, with 1.0 gram (0.003 mole) of 3-(5-amino-4-chloro-2-fluorophenyl)-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione, 0.5 mL (0.004 mole) of triethylamine, and 1.0 gram (0.004 mole) of 1-(benzylthiocarbonyl)ethylsulfonyl chloride in 10 mL of tetrahydrofuran as reagents. This preparation differed in that the reaction mixture was cooled to -70° C rather than 0° C. The yield of 3-[4-chloro-2-fluoro-5-[(1-benzylthiocarbonyl)ethylsulfonylamino]phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione was 0.4 gram, m.p. 73-78° C. The NMR spectrum was consistent with the proposed structure.

#### EXAMPLE 9

20           SYNTHESIS OF 3-[4-CHLORO-2-FLUORO-5-(N-METHOXY-N-METHYLAMINOCARBONYLMETHYLSULFONYLAMINO)PHENYL]-1-METHYL-6-TRIFLUOROMETHYL-2,4(1*H*,3*H*)-PYRIMIDINEDIONE (COMPOUND 17)

25           Step A           Synthesis of sodium N-methoxy-N-methylaminocarbonylmethylsulfonate and sodium chloride mixture as an intermediate

30           To stirred sodium sulfite, 10.0 grams (0.08 mole), was added 50 mL of water followed by 10.0 grams (0.07 mole) of 2-chloro-N-methoxy-N-methylacetamide. Upon completion of the addition the reaction mixture was stirred for 15 minutes and then heated to reflux, where it stirred for about 18 hours. After this time the reaction mixture was allowed to cool to ambient temperature and then poured into 500 mL of ethanol. The resulting mixture was cooled in the refrigerator for about 18 hours and then filtered through

diatomaceous earth. The filtrate was concentrated under reduced pressure, and the water remaining in the concentrate was removed by azeotroping with two 100 mL portions of ethanol, yielding 18.9 grams of organic product and sodium chloride. The NMR spectrum indicated the organic product to be sodium N-methoxy-N-methylaminocarbonylmethylsulfonate with a small amount of 2-chloro-N-methoxy-N-methylacetamide. The material was used in the next step without further purification.

Step B        Synthesis of N-methoxy-N-methylaminocarbonylmethylsulfonyl chloride as an intermediate

This compound was prepared in the manner of Step B, Example 7, with 30.0 mL (0.32 mole) of phosphorus oxychloride, 18.9 grams (0.06 mole) of sodium N-methoxy-N-methylaminocarbonylmethylsulfonate and sodium chloride mixture, and 100 mL of toluene. This preparation differed in that toluene was used in place of phosphorus pentachloride. The yield of N-methoxy-N-methylaminocarbonylmethylsulfonyl chloride was 7.5 grams. The NMR spectrum was consistent with the proposed structure.

Step C        Synthesis of 3-[4-chloro-2-fluoro-5-(N-methoxy-N-methylaminocarbonylmethylsulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione (Compound 17)

This compound was prepared in the manner of Step C, Example 7, with 1.0 gram (0.003 mole) of 3-(5-amino-4-chloro-2-fluorophenyl)-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione, 0.5 mL (0.004 mole) of triethylamine, and 0.7 gram (0.004 mole) of N-methoxy-N-methylaminocarbonylmethylsulfonyl chloride in 15 mL of tetrahydrofuran as reagents. This preparation differed in that the reaction mixture was cooled to -70° C rather than 0° C. The yield of 3-[4-chloro-2-fluoro-5-(N-methoxy-N-methylaminocarbonylmethylsulfonylamino)phenyl]-1-methyl-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione was 1.0 gram, m.p. 189-192° C. The NMR spectrum was consistent with the proposed structure.

## EXAMPLE 10

## SYNTHESIS OF 3-[4-CHLORO-5-(N,N-DIMETHYLAMINOSULFONYLAMINO)PHENYL]-1-AMINO-6-TRIFLUOROMETHYL-2,4(1H,3H)-PYRIMIDINEDIONE (COMPOUND 8)

5

Step A        Synthesis of 4-chloro-5-(N,N-dimethylaminosulfonylamino)-nitrobenzene as an intermediate

10        A stirred solution of about 1.0 grams (0.008 mole) of 4-dimethylaminopyridine and 15.0 (0.09 mole) of 5-amino-2-chloronitrobenzene in 60 mL of pyridine was cooled to -10° C to 0° C, and 10.0 mL (0.09 mole) of N,N-dimethylaminosulfonyl chloride was added dropwise during a 20-25 minute period. Upon completion of the addition the reaction mixture was allowed to warm to ambient temperature and then was heated to reflux, where it stirred

15        for about two hours. After this time the reaction mixture was analyzed by TLC, which indicated that the reaction was incomplete. The reaction mixture was stirred at reflux for about an additional 2.5 hours, after which the reaction mixture was again analyzed by TLC, which again indicated that the reaction was incomplete. The reaction mixture was stirred at reflux for an additional

20        15 minutes and then an additional 3.0 mL (0.03 mole) of 4-dimethylaminopyridine was added. Upon completion of this addition the reaction mixture was stirred at reflux for about an additional 18 hours. The reaction mixture was then analyzed by TLC for a third time, which indicated that only a small amount of starting material remained. The reaction mixture

25        was allowed to cool to ambient temperature and then poured into about 400 mL of aqueous 10% hydrochloric acid. The resulting solids were collected by filtration. The filter cake was washed with water and then with acetone, which dissolved some of the cake into the filtrate. The remaining filter cake was air-dried, yielding 9.2 grams of 4-chloro-5-(N,N-dimethylaminosulfonyl-

30        amino)nitrobenzene. The NMR spectrum was consistent with the proposed spectrum. The acetone was removed from the filtrate, and the resulting precipitate was collected by filtration. The filter cake was washed with water

and dried, yielding an 3.1 grams of crude product. This crude product was combined with 2.3 grams of crude product prepared by a similar route to yield a total of 5.4 grams of crude product.

5      **Step B      Synthesis of 4-chloro-5-(N,N-dimethylaminosulfonylamino)-aniline as an intermediate**

10      A solution of 8.2 grams (0.03 mole) of 4-chloro-5-(N,N-dimethylamino-sulfonylamino)nitrobenzene, 1.9 grams (0.04 mole) of ammonium chloride, 155 mL of ethanol, and 77 mL of water was stirred for ten minutes, and 10.7  
15      grams (0.19 mole) of iron powder was added in one portion. Upon completion of the addition the reaction mixture was heated to reflux, where it stirred for one hour. After this time the reaction mixture was cooled to ambient temperature and analyzed by TLC, which indicated the reaction was complete. The reaction mixture was filtered through diatomaceous earth,  
20      and the filtrate was concentrated under reduced pressure to a residue. The residue was taken up in ethyl acetate, washed with two 75 mL portions of water, dried with magnesium sulfate, and filtered. The filtrate was concentrated under reduced pressure, yielding 5.9 grams of 4-chloro-5-(N,N-dimethylaminosulfonylamino)aniline.

20      An additional 3.6 grams of 4-chloro-5-(N,N-dimethylaminosulfonylamino)aniline was prepared in the same manner. The NMR spectrum was consistent with the proposed structure.

25      **Step C      Synthesis of ethyl N-[4-chloro-5-(N,N-dimethylamino-sulfonylamino)phenyl]carbamate as an intermediate**

25      A stirred solution of 9.0 grams (0.04 mole) of 4-chloro-5-(N,N-dimethylaminosulfonylamino)aniline and 2.9 mL (0.04 mole) of pyridine in about 80 mL of methylene chloride was cooled to -15° C to -10° C, and 3.9  
30      grams (0.04 mole) of ethyl chloroformate was added during about a 20 minute period. Upon completion of the addition the reaction mixture was allowed to warm to ambient temperature, where it stirred for 45 minutes. After this time the reaction mixture was analyzed by TLC, which indicated the

reaction was complete. The reaction mixture was stirred at ambient temperature for an additional 18 hours. At the conclusion of this period the reaction mixture was transferred to a separatory funnel and washed with two portions of water. The organic layer was separated from the aqueous layer, dried with magnesium sulfate, and filtered. The filtrate was concentrated under reduced pressure, yielding 11.3 grams of a very tacky oil. This oil was triturated with pentane while warm, yielding 11.1 grams of ethyl N-[4-chloro-5-(N,N-dimethylaminosulfonylamino)phenyl]carbamate. The NMR spectrum was consistent with the proposed structure.

10    Step D        Synthesis of 3-[4-chloro-5-(N,N-dimethylaminosulfonylamino)-phenyl]-6-trifluoromethyl-2,4(1H,3H)-pyrimidinedione as an intermediate

Under a nitrogen atmosphere, a stirred solution of 0.8 grams (0.02 mole) of sodium hydride (60%) in 6 mL of N,N-dimethylformamide (DMF) was cooled to -3° C in an ice-bath, and 0.9 grams (0.005 mole) of ethyl 3-amino-4,4,4-trifluorocrotonate in 4 mL of DMF was added dropwise. The resulting mixture was allowed to warm to ambient temperature, and a solution of 1.5 grams (0.005 mole) of ethyl N-[4-chloro-5-(N,N-dimethylaminosulfonylamino)-phenyl]carbamate in 4 mL of DMF was added dropwise. Upon completion of the addition the reaction mixture was stirred for 15 minutes at ambient temperature and then heated to 125° C, where it stirred for an additional two hours. The reaction mixture was concentrated under reduced pressure to a residue, which was purified by column chromatography on silica gel. Elution was with a gradient of pure methylene chloride to 1:19 methanol and methylene chloride. The product-containing fractions were combined and concentrated under reduced pressure, yielding 1.0 gram of 3-[4-chloro-5-(N,N-dimethylaminosulfonylamino) phenyl]-6-trifluoromethyl-2,4(1H,3H)-pyrimidinedione, m.p. > 206° C. The NMR spectrum was consistent with the proposed structure.

An additional 2.9 grams of 3-[4-chloro-5-(N,N-dimethylaminosulfonylamino)-phenyl]-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione was prepared in the same manner.

5      Step E      Synthesis of 3-[4-chloro-5-(N,N-dimethylaminosulfonylamino)-phenyl]-1-amino-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione (Compound 8)

10      In order to effect solution a mixture of 0.8 gram (0.002 mole) of 3-[4-chloro-5-(N,N-dimethylaminosulfonylamino)phenyl]-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinedione and 0.5 gram (0.004 mole) of potassium carbonate in 25 mL of tetrahydrofuran was stirred at ambient temperature, and then 0.8 gram (0.004 mole) of 1-aminoxysulfonyl-2,4,6-trimethylbenzene was added in one portion. Upon completion of the addition the reaction mixture was stirred at ambient temperature for 1.5 hours. At the conclusion of this period  
15      the reaction mixture was poured into 75 mL of an aqueous saturated sodium chloride solution, and the resulting mixture was extracted with two 50 mL portions of ethyl acetate. The combined ethyl acetate extracts were washed with two portions of an aqueous saturated sodium chloride solution, dried with magnesium sulfate, and filtered. The filtrate was concentrated under  
20      reduced pressure, yielding 0.5 gram of 3-[4-chloro-5-(N,N-dimethylaminosulfonylamino)phenyl]-1-amino-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione, m.p. 203-204° C. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 11

25      SYNTHESIS OF 3-[4-CHLORO-2-FLUORO-5-(N,N-DIMETHYLAMINO-SULFONYLAMINO)PHENYL]-1-AMINO-6-TRIFLUOROMETHYL-2,4(1*H*,3*H*)-PYRIMIDINEDIONE (COMPOUND 10)

30      Step A      Synthesis of ethyl N-[2-fluoro-5-(N,N-dimethylaminosulfonylamino)phenyl]carbamate as an intermediate

This compound was prepared in the manner of Step A, Example 10, with 10.0 grams (0.05 mole) ethyl N-(5-amino-2-fluorophenyl)carbamate and

5.8 mL (0.05 mole) of N,N-dimethylsulfonyl chloride in 60 mL of pyridine as reagents. This preparation differed in that 4-dimethylaminopyridine was not used. The yield of ethyl N-[2-fluoro-5-(N,N-dimethylaminosulfonylamino)-phenyl]carbamate was 10.9 grams, m.p. 106.5-107.5° C. The NMR

5 spectrum was consistent with the proposed structure.

Step B          Synthesis of ethyl N-[4-chloro-2-fluoro-5-(N,N-dimethylamino-sulfonylamino)phenyl]carbamate as an intermediate

10          A stirred solution of 4.6 grams (0.02 mole) of ethyl N-[2-fluoro-5-(N,N-dimethylaminosulfonylamino)phenyl]carbamate in 60 mL of acetic acid and 6 mL of water was exposed to chlorine gas for five minutes. At the end of this period the reaction mixture was exposed to a nitrogen atmosphere for ten minutes, then analyzed by TLC, which indicated the reaction was complete. The reaction mixture was poured into 200 mL of water. The resulting solid  
15 was collected by filtration, yielding 4.1 grams of crude product. The crude product was purified by column chromatography on silica gel. Elution was accomplished with 1:1 hexane and ethyl acetate. The product-containing fractions were concentrated under reduced pressure, yielding 2.1 grams of  
20 ethyl N-[4-chloro-2-fluoro-5-(N,N-dimethylaminosulfonylamino) phenyl]-carbamate. The NMR spectrum was consistent with the proposed structure.

Step C          Synthesis of 3-[4-chloro-2-fluoro-5-(N,N-dimethylamino-sulfonylamino)phenyl]-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione as an intermediate

25          This compound was prepared in the manner of Step C, Example 10, with 2.4 grams (0.007 mole) of ethyl N-[4-chloro-2-fluoro-5-(N,N-dimethylamino-sulfonylamino)phenyl]carbamate, 1.2 grams (0.03 mole) of sodium hydride (60%), and 1.4 grams (0.008 mole) of ethyl 3-amino-4,4,4-trifluorocrotonate in 30 mL of N,N-dimethylformamide as reagents. The yield  
30 of 3-[4-chloro-2-fluoro-5-(N,N-dimethylaminosulfonylamino)phenyl]-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione was 0.9 gram, m.p. 79-81° C. The NMR spectrum was consistent with the proposed structure.

**Step D**      **Synthesis of 3-[4-chloro-2-fluoro-5-(N,N-dimethylamino-sulfonylamino)phenyl]-1-amino-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione (Compound 10)**

## EXAMPLE 13

5 SYNTHESIS OF 3-[4-CHLORO-2-FLUORO-5-[(N-2-CYANOETHYL-N-METHYLAMINO)SULFONYLAMINO]PHENYL]-1-METHYL-6-TRIFLUORO-METHYL-2,4(1H,3H)-PYRIMIDINEDIONE (COMPOUND 2)

Step A            Synthesis of N-2-cyanoethyl-N-methylaminosulfonyl chloride as an intermediate

10            A stirred solution of 4.0 mL (0.05 mole) of sulfuryl chloride in 15 mL of chloroform was cooled to -5° C, and 8.2 grams (0.10 mole) of 3-methylaminopropionitrile in 10 mL of chloroform was added dropwise at a rate to maintain the temperature below 0° C. Upon completion of addition, the reaction mixture was stirred for one hour and then allowed to warm to  
15            ambient temperature where it stirred for about 18 hours. After this time, the reaction mixture was filtered and washed with chloroform. The filtrate was concentrated under reduced pressure, yielding 4.8 grams of N-2-cyanoethyl-N-methylaminosulfonyl chloride. The NMR spectrum was consistent with the proposed structure.

20            Step B            Synthesis of 3-[4-chloro-2-fluoro-5-[(N-2-cyanoethyl-N-methyl-amino)sulfonylamino]phenyl]-1-methyl-6-trifluoromethyl-2,4-(1H,3H)-pyrimidinedione (Compound 2)

                 This compound was prepared in the manner of Example 4, with 0.6  
25            gram (0.002 mole) of 3-(5-amino-4-chloro-2-fluorophenyl)-1-methyl-6-trifluoromethyl-2,4(1H,3H)-pyrimidinedione, 0.2 gram (0.002 mole) of 4-dimethylaminopyridine, and 1.5 grams (0.008 mole) of N-2-cyanoethyl-N-methylaminosulfonyl chloride. The yield of 3-[4-chloro-2-fluoro-5-[(N-2-cyanoethyl-N-methylamino)sulfonylamino]phenyl]-1-methyl-6-trifluoromethyl-  
30            2,4(1H,3H)-pyrimidinedione was 0.3 gram, m.p. 123-126° C. The NMR spectrum was consistent with the proposed structure.

## EXAMPLE 14

SYNTHESIS OF 3-[4-CHLORO-2-FLUORO-5-(BENZYL SULFONYLAMINO)-  
PHENYL]-1-AMINO-6-TRIFLUOROMETHYL-2,4(1H,3H)-  
PYRIMIDINEDIONE (COMPOUND 19)

Step A      Synthesis of 4-chloro-2-fluoro-5-N,N-di(benzylsulfonyl)amino-  
nitrobenzene as an intermediate

This compound was prepared in the manner of Step C, Example 7, with 5.0 grams (0.03 mole) of 5-amino-4-chloro-2-fluoronitrobenzene, about 12.3 mL (0.09 mole) of triethylamine, and 15.7 grams (0.08 mole) of  $\alpha$ -toluenesulfonyl chloride in 135 mL of tetrahydrofuran as reagents. This preparation differed in that the reaction mixture was cooled to  $-55^{\circ}\text{C}$  to  $-50^{\circ}\text{C}$  rather than  $0^{\circ}\text{C}$ . The yield of 4-chloro-2-fluoro-5-N,N-di(benzylsulfonyl)-aminonitrobenzene was 11.6 grams. The NMR spectrum was consistent with the proposed structure.

Step B      Synthesis of 4-chloro-2-fluoro-5-(benzylsulfonylamino)nitrobenzene as an intermediate

To a stirred solution of 11.6 grams (0.02 mole) of 4-chloro-2-fluoro-5-N,N-di(benzylsulfonyl)aminonitrobenzene in 150 mL dioxane was added 30.0 mL (0.03 mole) of a 1N aqueous sodium hydroxide solution in one portion. Upon completion of the addition the reaction mixture was heated to  $66^{\circ}\text{C}$ , and an additional 17.0 mL (0.02 mole) of aqueous 1N sodium hydroxide solution was added. The reaction mixture was heated to  $70^{\circ}\text{C}$  during a 50 minute period, after which it was analyzed by TLC, which indicated the reaction was complete. The reaction mixture was allowed to cool to  $25^{\circ}\text{C}$ , and 25 mL of aqueous 2N hydrochloric acid was added. The resulting mixture was stirred at  $25^{\circ}\text{C}$  for 35 minutes, and then the acid and solvent were removed under reduced pressure to yield a residue, which was taken up in water and methylene chloride. The organic layer was separated, washed with two portions of aqueous 2N hydrochloric acid and one portion of

water, dried with magnesium sulfate, and filtered. The filtrate was concentrated under reduced pressure, yielding 7.5 grams of 4-chloro-2-fluoro-5-(benzylsulfonylamino)nitrobenzene, m.p. 136-141° C. The NMR spectrum was consistent with the proposed structure.

- 5           An additional 0.3 gram of 4-chloro-2-fluoro-5-(benzylsulfonylamino)-nitrobenzene was obtained by a similar route.

Step C       Synthesis of 4-chloro-2-fluoro-5-(benzylsulfonylamino)aniline as an intermediate

- 10           This compound was prepared in the manner of Step B, Example 10, with 0.6 gram (0.002 mole) of 4-chloro-2-fluoro-5-(benzylsulfonylamino)nitrobenzene, 0.1 gram (0.002 mole) of ammonium chloride, 0.6 gram (0.008 mole) of iron powder, 8 mL of ethanol, and 5 mL of water as reagents. The yield of 4-chloro-2-fluoro-5-(benzylsulfonylamino)aniline was 0.4 gram, m.p. 15 106-110° C. The NMR spectrum was consistent with the proposed structure.

An additional 4.0 grams of 4-chloro-2-fluoro-5-(benzylsulfonylamino)aniline was similarly prepared.

Step D       Synthesis of ethyl N-[4-chloro-2-fluoro-5-(benzylsulfonylamino)-phenyl]carbamate as an intermediate

- 20           This compound was prepared in the manner of Step C, Example 10, with 3.2 grams (0.01 mole) of 4-chloro-2-fluoro-5-(benzylsulfonylamino)aniline, 0.9 mL (0.01 mole) of pyridine, and 1.1 grams (0.01 mole) of ethyl chloroformate in 305 mL of methylene chloride as 25 reagents. The yield of ethyl N-[4-chloro-2-fluoro-5-(benzylsulfonylamino)phenyl]carbamate was 3.6 grams. The NMR spectrum was consistent with the proposed structure.

An additional 1.2 grams of ethyl N-[4-chloro-2-fluoro-5-(benzylsulfonylamino) phenyl]carbamate was prepared by a similar route.

Step E            Synthesis of 3-[4-chloro-2-fluoro-5-(benzylsulfonylamino)-phenyl]-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione as an intermediate

5            This compound was prepared in the manner of Step D, Example 10, with 2.6 grams (0.007 mole) of ethyl N-[4-chloro-2-fluoro-5-(benzylsulfonylamino) phenyl]carbamate, 0.5 gram (0.02 mole) of sodium hydride (60%), and 1.3 gram (0.008 mole) of ethyl 3-amino-4,4,4-trifluorocrotonate in 20 mL of N,N-dimethylformamide as reagents. The yield of 3-[4-chloro-2-fluoro-5-(benzylsulfonylamino)phenyl]-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione was 1.0 gram. The NMR spectrum was consistent with the proposed structure.

Step F            Synthesis of 3-[4-chloro-2-fluoro-5-(benzylsulfonylamino)-phenyl]-1-amino-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione (Compound 19)

15            This compound was prepared in the manner of Step E, Example 10, with 1.0 gram (0.002 mole) of 3-[4-chloro-2-fluoro-5-(benzylsulfonylamino)-phenyl]-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione, 0.3 gram (0.002 mole) of potassium carbonate, and 0.9 gram (0.004 mole) of 1-aminooxysulfonyl-2,4,6-trimethylbenzene in 25 mL of tetrahydrofuran as reagents. The yield of 3-[4-chloro-2-fluoro-5-(benzylsulfonylamino)phenyl]-6-trifluoromethyl-2,4(1*H*,3*H*)-pyrimidinedione was 0.3 gram. The NMR spectrum was consistent with the proposed structure.

#### 25            HERBICIDAL ACTIVITY

                 The 3-[2,4-disubstituted-5-(substituted amino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinediones of the present invention were tested for pre- and postemergence herbicidal activity on a variety of crops and weeds. The test plants included soybean (Glycine var. Winchester), field corn (Zea mays var. Pioneer 3732), wheat (Triticum aestivum var. Lew), morning-glory (Ipomea lacunosa or Ipomea hederacea), velvetleaf (Abutilon

theophrasti), green foxtail (Setaria viridis), Johnsongrass (Sorghum halepense), blackgrass (Alopecurus myosuroides), common chickweed (Stellaria media), and common cocklebur (Xanthium strumarium L.).

For preemergence testing two disposable fiber flats (8 cm x 15 cm x 25 cm) for each rate of application of each candidate herbicide were filled to an approximate depth of 6.5 cm with steam-sterilized sandy loam soil. The soil was leveled and impressed with a template to provide five evenly spaced furrows 13 cm long and 0.5 cm deep in each flat. Seeds of soybean, wheat, corn, green foxtail, and Johnsongrass were planted in the furrows of the first flat, and seeds of velvetleaf, morning-glory, common chickweed, cocklebur, and blackgrass were planted in the furrows of the second flat. The five-row template was employed to firmly press the seeds into place. A topping soil of equal portions of sand and sandy loam soil was placed uniformly on top of each flat to a depth of approximately 0.5 cm. Flats for postemergence testing were prepared in the same manner except that they were planted 9-14 days prior to the preemergence flats and were placed in a greenhouse and watered, thus allowing the seeds to germinate and the foliage to develop.

In both pre- and postemergence tests a stock solution of the candidate herbicide was prepared by dissolving 0.27g of the compound in 20 mL of water/acetone (50/50) containing 0.5% v/v sorbitan monolaurate. For an application rate of 3000 g/ha of herbicide a 10 mL portion of the stock solution was diluted with water/acetone (50/50) to 45 mL. The volumes of stock solution and diluent used to prepare solutions for lower application rates are shown in the following table:

Application Rate (g/ha)	Volume of Stock Solution (mL)	Volume of Acetone/Water (mL)	Total Volume of Spray Solution (mL)
3000	10	35	45
1000	3	42	45
300	1	44	45
100	0.3	45	45.3
30	0.1	45	45.1
10	0.03	45	45.03
3	0.01	45	45.01

The preemergence flats were initially subjected to a light water spray. The four flats were placed two by two along a conveyor belt (i.e., the two preemergence followed by the two postemergence flats). The conveyor belt fed under a spray nozzle mounted about ten inches above the postemergent foliage. The preemergence flats were elevated on the belt so that the soil surface was at the same level below the spray nozzle as the foliage canopy of the postemergent plants. The spray of herbicidal solution was turned on, and once it had stabilized the flats were passed under the spray at such a rate that they received a coverage equivalent of 1000L/ha. At this coverage the application rates are those shown in the above table for the individual herbicidal solutions. The preemergence flats were watered immediately thereafter, placed in the greenhouse, and watered regularly at the soil surface. The postemergence flats were immediately placed in the greenhouse and not watered until 24 hours after treatment with the test solution. Thereafter they were regularly watered at ground level. After 12-17 days the plants were examined and the phytotoxicity data were recorded.

Herbicidal activity data at selected application rates are given for various compounds of the present invention in Table 3 and Table 4. The test compounds are identified by numbers that correspond to those in Table 1.

- Phytotoxicity data are taken as percent control. Percent control is
- 5 determined by a method similar to the 0 to 100 rating system disclosed in "Research Methods in Weed Science," 2nd ed., B. Truelove, Ed.; Southern Weed Science Society; Auburn University, Auburn, Alabama, 1977. The rating system is as follows:

Herbicide Rating System

<u>Rating Percent Control</u>	<u>Description of Main Categories</u>	<u>Crop Description</u>	<u>Weed Description</u>
0	No effect	No crop reduction or injury	No weed control
10	Slight effect	Slight dis- coloration or stunting	Very poor weed control
20		Some dis- coloration, stunting or stand loss	Poor weed control
30		Crop injury more pronounced but not lasting	Poor to defi- cient weed control
40	Moderate effect	Moderate injury, crop usually recovers	Deficient weed control
50		Crop injury more lasting, recovery doubtful	Deficient to moderate weed control
60		Lasting crop injury, no recovery	Moderate weed control
70	Severe	Heavy injury and stand loss	Control some- what less than satisfactory
80		Crop nearly des- troyed, a few survivors	Satisfactory to good weed control
90		Only occasional live plants left	Very good to excellent control
100	Complete effect	Complete crop destruction	Complete weed destruction

For herbicidal application, the 3-[2,4-disubstituted-5-(substituted amino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinediones are formulated into herbicidal compositions by admixture in herbicidally effective amounts with adjuvants and carriers normally employed in the art for facilitating the dispersion of active ingredients for the particular utility desired, recognizing the fact that the formulation and mode of application of a toxicant may affect the activity of the material in a given application. Thus, for agricultural use the present herbicidal compounds may be formulated as granules of relatively large particle size, as water-soluble or water-dispersible granules, as powdery dusts, as wettable powders, as emulsifiable concentrates, as solutions, or as any of several other known types of formulations, depending on the desired mode of application.

These herbicidal compositions may be applied either as water-diluted sprays, or dusts, or granules to the areas in which suppression of vegetation is desired. These formulations may contain as little as 0.1%, 0.2% or 0.5% to as much as 95% or more by weight of active ingredient.

Dusts are free flowing admixtures of the active ingredient with finely divided solids such as talc, natural clays, kieselguhr, flours such as walnut shell and cottonseed flours, and other organic and inorganic solids which act as dispersants and carriers for the toxicant; these finely divided solids have an average particle size of less than about 50 microns. A typical dust formulation useful herein is one containing 1.0 part or less of the herbicidal compound and 99.0 parts of talc.

Wettable powders, also useful formulations for both pre- and post-emergence herbicides, are in the form of finely divided particles which disperse readily in water or other dispersants. The wettable powder is ultimately applied to the soil either as a dry dust or as an emulsion in water or other liquid. Typical carriers for wettable powders include Fuller's earth, kaolin clays, silicas, and other highly absorbent, readily wettable inorganic diluents. Wettable powders normally are prepared to contain about 5-80% of

active ingredient, depending on the absorbency of the carrier, and usually also contain a small amount of a wetting, dispersing or emulsifying agent to facilitate dispersion. For example, a useful wettable powder formulation contains 80.8 parts of the herbicidal compound, 17.9 parts of Palmetto clay, 1.0 part of sodium lignosulfonate, and 0.3 part of sulfonated aliphatic polyester as wetting agents. Frequently, additional wetting agent and/or oil will be added to the tank mix for postemergence application to facilitate dispersion on the foliage and absorption by the plant.

Other useful formulations for herbicidal applications are emulsifiable

concentrates (ECs) which are homogeneous liquid compositions dispersible in water or other dispersant, and may consist entirely of the herbicidal compound and a liquid or solid emulsifying agent, or may also contain a liquid carrier, such as xylene, heavy aromatic naphthas, isophorone, or other non-volatile organic solvent. For herbicidal application these concentrates are dispersed in water or other liquid carrier, and normally applied as a spray to the area to be treated. The percentage by weight of the essential active ingredient may vary according to the manner in which the composition is to be applied, but in general comprises 0.5 to 95% of active ingredient by weight of the herbicidal composition.

Flowable formulations are similar to ECs except that the active ingredient is suspended in a liquid carrier, generally water. Flowables, like ECs, may include a small amount of a surfactant, and contain active ingredient in the range of 0.5 to 95%, frequently from 10 to 50%, by weight of the composition. For application, flowables may be diluted in water or other liquid vehicle, and are normally applied as a spray to the area to be treated.

Typical wetting, dispersing or emulsifying agents used in agricultural formulations include, but are not limited to, the alkyl and alkylaryl sulfonates and sulfates and their sodium salts; alkylaryl polyether alcohols; sulfated higher alcohols; polyethylene oxides; sulfonated animal and vegetable oils; sulfonated petroleum oils; fatty acid esters of polyhydric alcohols and the

ethylene oxide addition products of such esters; and the addition product of long-chain mercaptans and ethylene oxide. Many other types of useful surface-active agents are available in commerce. The surface-active agent, when used, normally comprises from 1 to 15% by weight of the composition.

5 Other useful formulations include suspensions of the active ingredient in a relatively non-volatile solvent such as water, corn oil, kerosene, propylene glycol, or other suitable solvents.

Still other useful formulations for herbicidal applications include simple solutions of the active ingredient in a solvent in which it is completely soluble  
10 at the desired concentration, such as acetone, alkylated naphthalenes, xylene, or other organic solvents. Granular formulations, wherein the toxicant is carried on relatively coarse particles, are of particular utility for aerial distribution or for penetration of cover crop canopy. Pressurized sprays, typically aerosols wherein the active ingredient is dispersed in finely  
15 divided form by a propellant, such as carbon dioxide, propane or butane, may also be used. Water-soluble or water-dispersible granules are also useful formulations for herbicidal application of the present compounds. Such granular formulations are free-flowing, non-dusty, and readily water-soluble or water-miscible. The soluble or dispersible granular formulations  
20 described in U.S. patent No. 3,920,442 are useful herein with the present herbicidal compounds. In use by the farmer on the field, the granular formulations, emulsifiable concentrates, flowable concentrates, solutions, etc., may be diluted with water to give a concentration of active ingredient in the range of say 0.1% or 0.2% to 1.5% or 2%.

25 The 3-[2,4-disubstituted-5-(substituted amino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinediones of this invention may be formulated and/or applied with insecticides, fungicides, nematocides, plant growth regulators, fertilizers, or other agricultural chemicals and may be used as effective soil sterilants as well as selective herbicides in agriculture. In  
30 applying an active compound of this invention, whether formulated alone or

with other agricultural chemicals, an effective amount and concentration of the active compound is of course employed; the amount may be as low as, for example, about 3 to 3000 g/ha to, preferably, about 10 to 30 g/ha. For field use, where there are losses of herbicide, higher application rates (for example, four times the rates mentioned above) may be employed.

The 3-[2,4-disubstituted-5-(substituted amino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinediones of this invention may be used in combination with other herbicides, for example they may be mixed with, say, an equal or larger amount of a known herbicide such as aryloxyalkanoic acid herbicides such as (2,4-dichlorophenoxy)acetic acid (2,4-D), (4-chloro-2-methylphenoxy)acetic acid (MCPA), (+/-)-2-(4-chloro-2-methylphenoxy)propanoic acid (MCPA); urea herbicides, such as N,N-dimethyl-N'-[4-(1-methylethyl)phenyl]urea (isoproturon); imidazolinone herbicides, such as 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-3-pyridinecarboxylic acid (imazapyr), a reaction product comprising (+/-)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-4-methylbenzoic acid and (+/-)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-5-methylbenzoic acid (imazamethabenz), (+/-)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-5-ethyl-3-pyridinecarboxylic acid (imazethapyr), and (+/-)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-3-quinolinecarboxylic acid (imazaquin); diphenyl ether herbicides, such as 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoic acid (acifluorfen), methyl 5-(2,4-dichlorophenoxy)-2-nitrobenzoate (bifenox), and 5-[2-chloro-4-(trifluoromethyl)phenoxy]-N-(methylsulfonyl)-2-nitrobenzamide (fomazafen); hydroxybenzoxazole herbicides, such as 4-hydroxy-3,5-diiodobenzoxazole (ioxynil), and 3,5-dibromo-4-hydroxybenzoxazole (bromoxynil); sulfonylurea herbicides, such as 2-[[[(4-chloro-6-methoxy-2-pyrimidinyl)-amino]carbonyl]amino]sulfonyl]benzoic acid (chlorimuron), 2-chloro-N-[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide (chlorsulfuron), 2-[[[(4,6-dimethoxy-

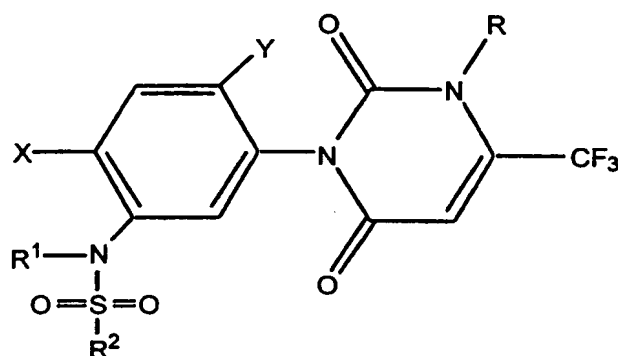
2-pyrimidinyl)aminocarbonyl]amino]-sulfonyl]methyl]benzoic acid  
(bensulfuron), 2-[[[[(4,6-dimethoxy-2-pyrimidin-yl)amino]carbonyl]amino]-  
sulfonyl]-1-methyl-1H-pyrazol-4-carboxylic acid (pyrazosulfuron), 3-[[[[(4-  
methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]-amino]sulfonyl]-2-  
5 thiophenecarboxylic acid (thifensulfuron), and 2-(2-chloroethoxy)-N-[[[(4-  
methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]-benzene-sulfonamide  
(triasulfuron); 2-(4-aryloxyphenoxy)alkanoic acid herbicides, such as (+/-)-2-  
[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]propanoic acid (fenoxaprop), (+/-)-  
2-[4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]phenoxy]propanoic acid (fluazifop),  
10 (+/-)-2-[4-(6-chloro-2-quinoxalinyloxy]phenoxy]propanoic acid (quizalofop),  
and (+/-)-2-[-(2,4-dichlorophenoxy)phenoxy]propanoic acid (diclofop);  
benzothiadiazinone herbicides, such as 3-(1-methylethyl)-1H-2,1,3-  
benzothiadiazin-4(3H)-one 2,2-dioxide (bentazone); 2-chloroacetanilide  
herbicides, such as N-(butoxymethyl)-2-chloro-2',6'-diethylacetanilide  
15 (butachlor); arenecarboxylic acid herbicides, such as 3,6-dichloro-2-  
methoxybenzoic acid (dicamba); and pyridyloxyacetic acid herbicides, such  
as [(4-amino-3,5-dichloro-6-fluoro-2-pyridinyl)oxy]-acetic acid (fluroxypyr).

It is apparent that various modifications may be made in the  
formulation and application of the compounds of this invention without  
20 departing from the inventive concepts herein as defined in the claims.

Table 1

3-[2,4-Disubstituted-5-(substituted amino)phenyl]-1-substituted-6-trifluoromethyl-2,4-(1*H*,3*H*)-pyrimidinediones as Herbicides

5



Cmpd. No.	R	R¹	R²	X	Y
1	-CH₃	H		Cl	F
2	-CH₃	H	-N(CH₃)CH₂CH₂C≡N	Cl	F
3	-CH₃	H	-N(CH₃)₂	-CH₃	F
4	-CH₃	-C(O)CH₂OC(O)CH₃	-N(CH₃)₂	Cl	F
5	-CH₃	-C(O)CH₂OC(O)CH₃	-	Cl	F
6	-CH₃	-C(O)CH₂OC(O)CH₃	N(CH₃)C(O)CH₂OC(O)CH₃	Cl	F
7	-NH₂	H	-CH(CH₃)C≡N	Cl	H
8	-NH₂	H	-N(CH₃)₂	Cl	H

Table 1 (continued)

Cmpd. No.	R	R <sup>1</sup>	R <sup>2</sup>	X	Y
9	-NH <sub>2</sub>	H	-CH(CH <sub>3</sub> )C≡N	Cl	F
10	-NH <sub>2</sub>	H	-N(CH <sub>3</sub> ) <sub>2</sub>	Cl	F
11	-CH <sub>3</sub>	H	-CH <sub>2</sub> CH <sub>2</sub> OC <sub>6</sub> H <sub>5</sub>	Cl	F
12	-CH <sub>3</sub>	H	-CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> OC <sub>6</sub> H <sub>5</sub>	Cl	F
13	-CH <sub>3</sub>	H	-CH <sub>2</sub> CH(CH <sub>3</sub> )C≡N	Cl	F
14	-CH <sub>3</sub>	H	-CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> C≡N	Cl	F
15	-CH <sub>3</sub>	S(O) <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> C≡N	-CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> C≡N	Cl	F
16	-CH <sub>3</sub>	H	-CH <sub>2</sub> C(O)N(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	Cl	F
17	-CH <sub>3</sub>	H	-CH <sub>2</sub> C(O)N(CH <sub>3</sub> )OCH <sub>3</sub>	Cl	F
18	-CH <sub>3</sub>	H	-CH <sub>2</sub> C(O)OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	Cl	F
19	-NH <sub>2</sub>	H	-CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	Cl	F
20	-CH <sub>3</sub>	H	-NHCH <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	Cl	F
21	-CH <sub>3</sub>	H	-N(CH <sub>3</sub> )CH <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	Cl	F
22	-CH <sub>3</sub>	H	$  \begin{array}{c}  \text{CH}_2\text{CH}_2\text{CH}_3 \\  \diagup \\  \text{---N---} \\  \diagdown \\  \text{CH-C}\equiv\text{N} \\    \\  \text{CH}_3  \end{array}  $	Cl	F
23	-CH <sub>3</sub>	H	-N(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> OC <sub>6</sub> H <sub>5</sub>	Cl	F

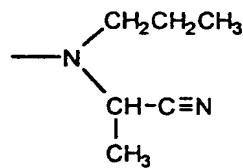
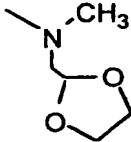


Table 1 (continued)

Cmpd. No.	R	R'	R <sup>2</sup>	X	Y
24	-CH <sub>3</sub>	H	-N(CH <sub>2</sub> C≡N)CH <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	Cl	F
25	-CH <sub>3</sub>	H	$  \begin{array}{c}  \text{H}_3\text{C} \quad \text{CH}_3 \\  \quad \diagdown \quad \diagup \\  \quad \text{CH} \\  \quad   \\  \text{---N---CH---C}\equiv\text{N} \\    \\  \text{H}  \end{array}  $	Cl	F
26	-NH <sub>2</sub>	H	-N(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	Cl	F
27	-CH <sub>3</sub>	H	-CH <sub>2</sub> CONH <sub>2</sub>	Cl	F
28	-CH <sub>3</sub>	H	-CH <sub>2</sub> CONHCH <sub>3</sub>	Cl	F
29	-CH <sub>3</sub>	H	-CH <sub>2</sub> CON(CH <sub>3</sub> ) <sub>2</sub>	Cl	F
30	-CH <sub>3</sub>	H	-CH <sub>2</sub> C(O)NHCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	Cl	F
31	-CH <sub>3</sub>	H	-CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> C≡N	Cl	F
32	-CH <sub>3</sub>	H	-CH <sub>2</sub> CO <sub>2</sub> CH(CH <sub>3</sub> ) <sub>2</sub>	Cl	F
33	-CH <sub>3</sub>	H	-CH <sub>2</sub> CO <sub>2</sub> CH <sub>2</sub> C≡N	Cl	F
34	-CH <sub>3</sub>	H	-CH <sub>2</sub> CO <sub>2</sub> CH <sub>2</sub> C≡CH	Cl	F
35	-CH <sub>3</sub>	H	-CH <sub>2</sub> CO <sub>2</sub> CH <sub>2</sub> C(CH <sub>3</sub> )=CH <sub>2</sub>	Cl	F
36	-CH <sub>3</sub>	H	-CH <sub>2</sub> CH(CH <sub>3</sub> )CON(CH <sub>3</sub> ) <sub>2</sub>	Cl	F
37	-CH <sub>3</sub>	-CH <sub>3</sub>	-N(CH <sub>3</sub> )C <sub>2</sub> H <sub>4</sub> C≡N	Cl	F
38	-CH <sub>3</sub>	-C(O)CH <sub>3</sub>	-N(CH <sub>3</sub> )C <sub>2</sub> H <sub>4</sub> C≡N	Cl	F

Table 1 (continued)

Cmpd. No.	R	R <sup>1</sup>	R <sup>2</sup>	X	Y
39	-CH <sub>3</sub>	-C(O)OCH <sub>3</sub>	-N(CH <sub>3</sub> )C <sub>2</sub> H <sub>4</sub> C≡N	Cl	F
40	-CH <sub>3</sub>	-C(O)CH <sub>2</sub> OC(O)CH <sub>3</sub>	-N(CH <sub>3</sub> )C <sub>2</sub> H <sub>4</sub> C≡N	Cl	F
41	-CH <sub>3</sub>	-C(O)CH <sub>2</sub> OC(O)CH <sub>3</sub>	-C <sub>2</sub> H <sub>5</sub>	Cl	F
42	-CH <sub>3</sub>	-C(O)CH <sub>2</sub> OC(O)CH <sub>3</sub>	-CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	Cl	F
43	-CH <sub>3</sub>	-C(O)CH <sub>3</sub>	-CH <sub>2</sub> C(O)N(CH <sub>3</sub> )OCH <sub>3</sub>	Cl	F
44	-CH <sub>3</sub>	-S(O) <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> C≡N	-CH <sub>2</sub> CH <sub>2</sub> C≡N	Cl	F
45	-CH <sub>3</sub>	H	-CH <sub>2</sub> CH <sub>2</sub> C≡N	Cl	F
46	-CH <sub>3</sub>	H	-N(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> C≡N	Cl	H
47	-CH <sub>3</sub>	H	-N(CH <sub>3</sub> )C(O)CH <sub>2</sub> OC(O)CH <sub>3</sub>	Cl	F
48	-CH <sub>3</sub>	H		Cl	F
49	-CH <sub>3</sub>	H	2-(2-chlorophenoxy)ethyl	Cl	F
50	-CH <sub>3</sub>	H	2-(4-chlorophenoxy)ethyl	Cl	F

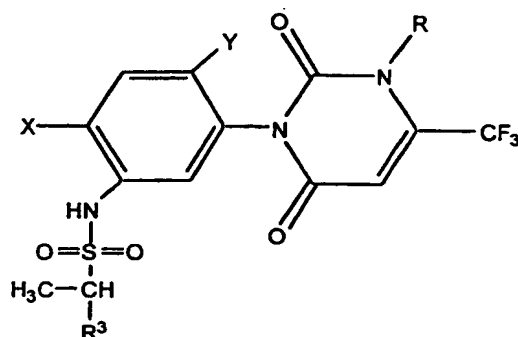


Table 1 (continued)

Cmpd. No.	R	R <sup>3</sup>	X	Y
51	-CH <sub>3</sub>	-C(O)N(CH <sub>3</sub> )OCH <sub>3</sub>	Cl	F
52	-CH <sub>3</sub>	-C(O)NHC <sub>6</sub> H <sub>5</sub>	Cl	F
53	-CH <sub>3</sub>	-C(O)SCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	Cl	F
54	-CH <sub>3</sub>	-NO <sub>2</sub>	Cl	F
55	-CH <sub>3</sub>	-CO <sub>2</sub> H	Cl	F
56	-CH <sub>3</sub>	-CONH <sub>2</sub>	Cl	F
57	-CH <sub>3</sub>	-CONHCH <sub>3</sub>	Cl	F
58	-CH <sub>3</sub>	-CON(CH <sub>3</sub> ) <sub>2</sub>	Cl	F
59	-CH <sub>3</sub>	-COSC <sub>2</sub> H <sub>5</sub>	Cl	F
60	-CH <sub>3</sub>		Cl	F
61	-NH <sub>2</sub>	-CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	Cl	F
62	-NH <sub>2</sub>	-C(O)N(CH <sub>3</sub> )OCH <sub>3</sub>	Cl	F

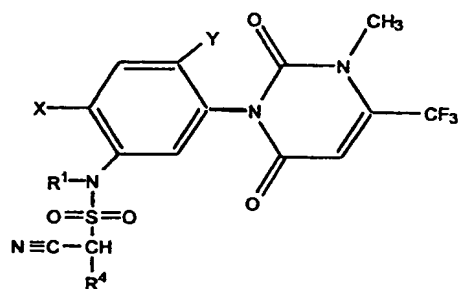


Table 1 (continued)

Cmpd. No.	R <sup>1</sup>	R <sup>4</sup>	X	Y
63	H	H	Cl	H
64	H	H	Cl	F
65	H	H	Br	F
66	H	-CH <sub>3</sub>	Cl	H
67	H	-CH <sub>3</sub>	Cl	Cl
68	H	-CH <sub>3</sub>	Cl	F
69	H	-CH <sub>3</sub>	Br	F
70	H	-C <sub>2</sub> H <sub>5</sub>	Cl	H
71	H	-C <sub>2</sub> H <sub>5</sub>	Cl	F

Table 1 (continued)

Cmpd. No.	R <sup>1</sup>	R <sup>4</sup>	X	Y
72	H	-C <sub>2</sub> H <sub>5</sub>	Br	F
73	H	-CH(CH <sub>3</sub> ) <sub>2</sub>	Cl	H
74	H	-CH(CH <sub>3</sub> ) <sub>2</sub>	Cl	F
75	H	-CH(CH <sub>3</sub> ) <sub>2</sub>	Br	F
76	H	-C <sub>3</sub> H <sub>7</sub>	Cl	F
77	H	-CHClC <sub>6</sub> H <sub>5</sub>	Cl	F
78	-CH <sub>3</sub>	-CH <sub>3</sub>	Cl	F
79	-C(O)CH <sub>3</sub>	-CH <sub>3</sub>	Cl	F

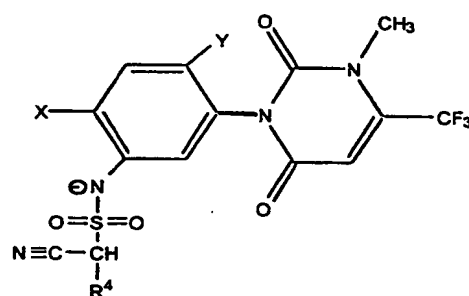
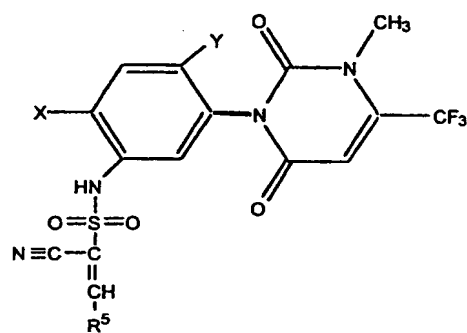
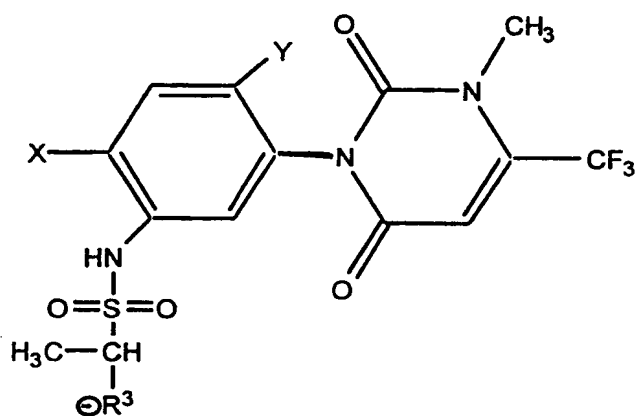


Table 1 (continued)

Cmpd. No.	R <sup>4</sup>	X	Y
80 (Sodium Salt)	-CH <sub>3</sub>	Cl	F
81 (Isopropylamine Salt)	-CH <sub>3</sub>	Cl	F
82 (Sodium Salt)	-C <sub>2</sub> H <sub>5</sub>	Cl	F



Cmpd. No.	R <sup>5</sup>	X	Y
83	phenyl	Cl	H
84	furan-2-yl	Cl	F



Cmpd. No.	R <sup>3</sup>	X	Y
85 (Sodium Salt)	-CO <sub>2</sub>	Cl	F

Table 2  
CHARACTERIZING DATA

<u>Cmpd No</u>	<u>Melting Point/Physical State</u>	<u>Cmpd No</u>	<u>Melting Point/Physical State</u>
1	202-204 °C	48	RESIN
2	123-126 °C	49	67-72 °C w/prior sintering
3	SOLID	50	73-76 °C w/prior sintering
4	80-81 °C becomes resin	51	95-96 °C
5	SOLID	52	127-128 °C
6	100-106 °C	53	73-78 °C
7	> 207 °C	58	92-98 °C
8	203-204 °C	62	96-99 °C w/prior sintering
9	124-125 °C becomes resin	63	220-223 °C
10	SOLID	64	100-102 °C
11	70-73 °C	65	119-120 °C
12	80-83 °C becomes resin	66	solid
13	79-80 °C	67	105-108 °C
14	SOLID	68	97-105 °
15	217-220 °C	69	108-110 °C
16	190-193 °C	70	114-115 °C
17	SOLID	71	94-98 °C
18	64-69 °C	72	87-88 °C
19	SOLID	73	95-100 °C
21	WAXY RESIN	74	SOLID
29	206-208 °C	75	95-97 °C
37	65-68 °C w/prior sintering	76	86-87 °C
38	SOLID	77	188-190 °C
39	SOLID	78	SOLID
40	SOLID	79	108-112 °C
41	160-161 °C w/prior sintering	80	SOLID
42	174-175 °C	81	SOLID
43	91-92 °C becomes resin	82	SOLID
44	125-126 °C	83	SOLID
45	91-92 °C	84	72-73 °C
46	170-172 °C		
47	SOLID		

Table 3  
PREEMERGENCE HERBICIDAL ACTIVITY (% CONTROL)

<u>Cmpd</u>											
<u>No.</u>	<u>Rate</u>	<u>Soy</u>	<u>Wht</u>	<u>Cm</u>	<u>Abuth</u>	<u>Iposs</u>	<u>Sterne</u>	<u>Xanpe</u>	<u>Alomy</u>	<u>Setvi</u>	<u>Sorha</u>
1	0.3	40	10	20	100	100	70	20	60	60	40
2	0.3	75	40	50	100	100	100	100	60	50	55
3	0.3	100	60	80	100	100	100	60	55	100	80
4	0.3	100	90	90	100	100	100	100	80	100	80
5	0.3	60	60	80	100	100	100	80	60	80	80
6	0.3	50	60	50	100	100	100	100	65	60	75
7	0.3	100	10	0	100	100	100	90	20	100	30
8	0.3	100	75	90	100	100	100	100	70	100	75
9	0.3	100	60	60	100	100	100	100	75	100	65
10	0.3	100	80	90	100	100	100	100	80	100	85
11	0.3	80	20	40	100	100	100	90	80	90	50
12	0.3	100	25	10	100	100	100	90	60	70	70
13	0.3	30	20	20	100	100	100	100	70	90	40
14	0.3	80	50	60	100	100	100	100	90	90	70
15	0.3	40	0	10	100	100	90	100	70	60	55
16	0.3	60	0	20	100	100	ND	70	50	0	30
17	0.3	90	30	60	100	100	100	100	80	40	75
18	0.3	25	10	20	100	100	100	50	30	20	50
19	0.3	100	80	90	100	100	ND	100	90	100	85
21	0.3	95	50	50	100	100	100	100	75	90	75
29	0.3	60	20	60	100	100	100	100	80	40	80
37	0.3	100	100	80	100	100	100	100	100	100	80
38	0.3	100	40	80	100	100	100	100	95	90	75
39	0.3	100	100	100	100	100	100	100	100	100	100
40	0.3	100	30	60	100	100	100	100	80	100	65
41	0.3	80	80	80	100	100	100	ND	ND	100	100
42	0.3	20	50	70	100	100	100	ND	ND	50	50
44	0.3	95	30	60	100	100	100	100	ND	80	80
45	0.3	80	30	40	100	100	100	100	ND	90	80
46	0.3	80	0	30	100	100	100	100	ND	70	30
47	0.3	30	50	75	100	100	90	ND	ND	80	70
48	0.3	100	70	90	100	95	100	100	ND	95	90

Table 3 (continued)

Cmpd

<u>No.</u>	<u>Rate</u>	<u>Soy</u>	<u>Wht</u>	<u>Cm</u>	<u>Abuth</u>	<u>Ipss</u>	<u>Steme</u>	<u>Xanpe</u>	<u>Alomy</u>	<u>Setvi</u>	<u>Sorha</u>
49	0.3	100	40	10	100	100	ND	80	90	80	60
50	0.3	20	40	0	100	100	ND	100	100	70	25
51	0.3	60	60	60	100	100	70	90	80	65	65
52	0.3	100	10	20	100	100	100	100	50	40	25
53	0.3	60	10	25	100	100	100	80	60	95	70
58	0.3	95	80	80	100	100	100	100	80	95	90
62	0.3	100	80	90	100	100	100	100	ND	100	100
63	0.3	10	10	10	100	100	100	100	60	60	20
64	0.3	100	70	60	100	100	100	100	75	80	75
65	0.3	50	25	20	100	100	80	90	ND	80	70
66	0.3	0	10	0	100	100	ND	100	ND	25	30
67	0.3	40	10	20	90	100	50	50	20	30	50
68	0.3	70	60	40	100	100	100	100	ND	65	65
69	0.3	20	40	20	100	100	100	100	ND	80	70
70	0.3	10	0	25	100	100	100	100	40	70	50
71	0.3	80	50	60	100	100	ND	100	ND	60	90
72	0.3	40	60	25	100	100	100	100	80	100	75
73	0.3	0	0	10	100	100	95	100	30	0	30
74	0.3	35	10	20	100	100	90	100	50	25	60
75	0.3	0	30	10	100	100	100	100	10	10	40
76	0.3	80	60	40	100	100	100	100	75	100	80
77	0.3	20	10	20	100	100	55	60	25	50	40
78	0.3	100	70	90	100	100	80	100	75	100	100
79	0.3	95	50	10	100	100	100	100	80	90	80
80	0.3	70	30	20	100	100	100	100	80	100	60
81	0.3	90	50	30	100	100	100	100	90	100	90
82	0.3	5	50	15	100	100	ND	100	ND	70	40
83	0.3	0	40	10	100	100	100	100	40	25	20
84	0.3	50	30	10	100	100	ND	80	ND	70	60

Rate is in kg/hectare. Soy is soybean; Wht, wheat; Cm, corn; Abuth, velvetleaf; Ipss, morning-glory; Steme, chickweed; Xanpe, cocklebur; Alomy, blackgrass;

5 Setvi, green foxtail; Sorha, Johnsongrass

ND = NO DATA

Table 4  
POSTEMERGENCE HERBICIDAL ACTIVITY (% CONTROL)

<u>Cmpd</u>											
<u>No.</u>	<u>Rate</u>	<u>Soy</u>	<u>Wht</u>	<u>Cm</u>	<u>Abuth</u>	<u>Ipss</u>	<u>Steme</u>	<u>Xanpe</u>	<u>Alomy</u>	<u>Setvi</u>	<u>Sorha</u>
1	0.3	70	30	50	100	100	25	40	20	70	40
2	0.3	90	35	70	100	100	100	100	60	70	60
3	0.3	80	50	75	100	80	75	100	50	80	70
4	0.3	90	70	80	100	100	100	100	90	70	70
5	0.3	80	60	60	100	100	80	95	40	80	60
6	0.3	75	40	80	100	100	100	100	60	80	60
7	0.3	80	40	65	100	100	100	100	50	100	60
8	0.3	90	70	80	100	100	100	100	70	100	80
9	0.3	85	40	80	100	100	100	100	70	100	70
10	0.3	90	100	90	100	100	100	100	100	100	95
11	0.3	95	35	70	100	100	100	100	60	70	65
12	0.3	80	30	70	100	100	100	100	50	70	60
13	0.3	80	35	80	100	100	100	100	70	70	75
14	0.3	90	40	70	100	100	100	100	80	80	90
15	0.3	80	25	60	100	100	100	100	40	60	30
16	0.3	70	40	70	100	100	100	100	70	70	5
17	0.3	70	35	75	100	100	100	100	65	70	80
18	0.3	70	40	50	100	100	30	50	30	60	50
19	0.3	80	80	80	100	100	100	100	90	100	90
21	0.3	90	40	70	100	100	70	100	60	100	60
29	0.3	70	50	60	100	100	95	100	50	90	60
37	0.3	90	40	70	100	100	100	ND	80	90	70
38	0.3	95	50	70	100	100	100	ND	80	70	50
39	0.3	95	80	90	100	100	100	100	80	100	100
40	0.3	80	40	70	100	100	100	ND	75	80	45
41	0.3	70	80	75	100	100	100	100	ND	100	90
42	0.3	70	50	70	100	100	100	100	ND	60	40
44	0.3	90	30	70	100	100	100	ND	ND	60	50
45	0.3	90	60	80	100	100	100	100	ND	100	70
46	0.3	90	35	60	100	100	100	95	ND	40	20
47	0.3	70	40	70	100	100	95	100	ND	40	50
48	0.3	95	60	80	100	100	100	95	ND	80	70

Table 4 (continued)

Cmpd

<u>No.</u>	<u>Rate</u>	<u>Soy</u>	<u>Wht</u>	<u>Crn</u>	<u>Abuth</u>	<u>Iposs</u>	<u>Steme</u>	<u>Xanpe</u>	<u>Alomy</u>	<u>Setvi</u>	<u>Sorha</u>
49	0.3	90	30	80	100	100	ND	ND	60	100	40
50	0.3	95	25	75	100	100	ND	100	ND	100	40
51	0.3	80	60	80	100	100	100	100	75	80	95
52	0.3	80	40	80	100	100	90	100	40	60	70
53	0.3	65	20	60	100	100	90	100	40	90	70
58	0.3	90	60	60	100	100	100	100	100	95	80
62	0.3	100	70	90	100	100	100	100	95	100	100
63	0.3	70	50	60	100	100	100	95	50	50	60
64	0.3	75	50	70	100	100	100	100	50	50	60
65	0.3	75	50	70	100	100	100	100	ND	90	70
66	0.3	70	40	50	100	100	100	100	ND	75	50
67	0.3	60	50	80	80	100	20	95	10	20	40
68	0.3	80	40	80	100	100	100	100	ND	75	70
69	0.3	80	50	80	100	100	100	100	ND	60	60
70	0.3	70	20	70	100	100	100	100	60	80	50
71	0.3	80	40	80	100	100	100	100	ND	80	70
72	0.3	75	40	80	100	100	ND	100	70	100	80
73	0.3	70	40	70	100	100	100	100	20	ND	40
74	0.3	70	40	70	100	100	100	100	40	ND	60
75	0.3	70	30	80	100	100	100	100	50	ND	60
76	0.3	70	30	80	100	100	100	100	70	100	90
77	0.3	60	40	90	100	100	50	80	50	100	60
78	0.3	90	40	70	100	100	80	80	60	100	80
79	0.3	80	50	90	100	100	100	100	70	75	90
80	0.3	75	40	70	100	100	100	100	40	80	70
81	0.3	75	30	70	100	100	100	100	70	90	70
82	0.3	75	40	70	100	100	100	100	ND	50	50
83	0.3	50	20	40	70	90	60	70	30	20	30
84	0.3	70	30	60	100	100	ND	90	ND	80	40

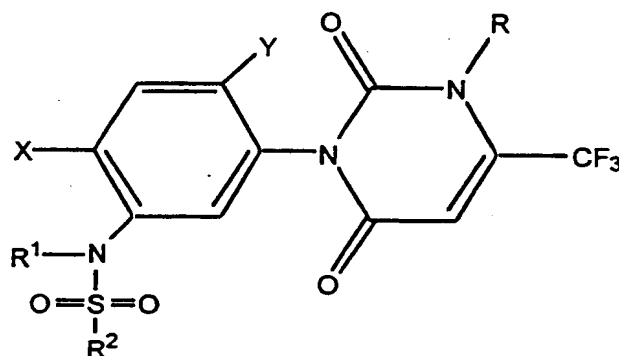
Rate is in kg/hectare. Soy is soybean; Wht, wheat; Crn, corn; Abuth, velvetleaf;  
Iposs, morning-glory; Steme, chickweed; Xanpe, cocklebur; Alomy, blackgrass;

5 Setvi, green foxtail; Sorha, Johnsongrass

ND = NO DATA

**Claims:**

1. A compound of the formula



- 5 in which:

X and Y are independently selected from hydrogen, halogen, and alkyl;

R is alkyl or amino;

- R<sup>1</sup> is hydrogen, alkyl, cyanoalkylsulfonyl, acyl, acyloxyacyl, alkoxycarbonyl, or represents the negative charge of the anion of a salt;  
 10 R<sup>2</sup> is:

(1) alkyl, cyanoalkyl, cyanoalkoxycarbonylalkyl, alkenoxycarbonylalkyl, alkynoxycarbonylalkyl, arylalkyl, aryloxyalkyl, arylalkoxycarbonylalkyl, heterocyclyl, amino, aminocarbonylalkyl;

- 15 (2) —W—R<sup>3</sup> in which W is alkyl, and R<sup>3</sup> is aminocarbonyl, alkoxycarbonyl, hydroxycarbonyl, arylalkylthiocarbonyl, nitro, alkylthiocarbonyl, or heterocyclylalkoxycarbonyl;

(3) —CH(C≡N)R<sup>4</sup>, in which R<sup>4</sup> is hydrogen, alkyl, arylalkyl, or arylhaloalkyl; or

- 20 (4) —C(C≡N)=CHR<sup>5</sup>; in which R<sup>5</sup> is aryl or heterocyclyl;

with the proviso that an amino group may be substituted with one or two substituents independently selected from alkyl, cyanoalkyl, alkoxy, alkoxycarbonylalkyl, acyloxyacyl, aryl, arylalkyl, aryloxyalkyl, and heterocyclylalkyl; halogen is chlorine, bromine, or fluorine; the alkyl and acyl

moieties may each contain 1-6 carbon atoms, the alkenyl and alkynyl moieties may each contain 2-6 carbon atoms, each may be straight or branched, and the total number of carbon atoms in any  $R^1$ ,  $R^2$ ,  $R^3$ , or  $R^4$  does not exceed 12; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with halogen; and heterocyclyl is selected from 2,3-dihydro-2,2-dimethylbenzofuran-7-yl and 1,3-dioxolan-2-yl;

with the further proviso that when  $R^2$  is amino, alkylamino, dialkylamino, arylamino, or arylalkylamino, and R is alkyl,  $R^1$  is not hydrogen, alkyl, alkylcarbonyl, or alkoxycarbonyl; and

- 10           when  $R^2$  is arylalkyl, or alkoxycarbonylalkyl, and R is alkyl,  $R^1$  cannot be hydrogen, alkyl, alkylcarbonyl, or alkoxycarbonyl, but may be alkyl only when is cyanoalkylsulfonyl or acyloxyacyl; or the sodium, potassium or 1-8 carbon amine salts thereof.

2. A compound of claim 1 in which:

- 15           R is alkyl or amino;

$R^1$  is hydrogen, alkyl, acyl, acyloxyacyl, or represents the negative charge of the anion of a salt;

$R^2$  is

- 20           (1) cyanoalkyl, aryloxyalkyl, amino, or aminocarbonylalkyl, in which an amino group may be substituted with one or two substituents independently selected from alkyl, cyanoalkyl, or alkoxy;

with the proviso that when  $R^2$  is amino, alkylamino, or dialkylamino, and R is alkyl,  $R^1$  is not hydrogen or alkyl; or

(2)  $-\text{CH}(\text{C}\equiv\text{N})\text{R}^4$ , in which  $R^4$  is hydrogen or alkyl;

- 25           with the proviso that the alkyl, alkoxy, and acyl moieties may each contain 1-4 carbon atoms; each may be straight or branched; the total number of carbon atoms in any  $R^1$ ,  $R^2$ , or  $R^4$  is does not exceed 8; and aryl is selected from phenyl or furanyl.

3. A compound of claim 2 in which

X is chlorine or bromine;

Y is hydrogen or fluorine;

R is methyl or amino;

5 R<sup>1</sup> is hydrogen, acetyl, or acetoxyacetyl;

R<sup>2</sup> is

(1) 1-cyanoethyl, 2-cyanopropyl, phenoxyethyl, dimethylamino,  
(2-cyanoethyl)(methyl)amino, or aminocarboxymethyl, in which an amino  
group may be substituted with one or two substituents independently

10 selected from methyl, methoxy, phenyl, or benzyl;

with the proviso that when R<sup>2</sup> is dimethylamino, and R is methyl, R<sup>1</sup> is  
not hydrogen; or

(2) —CH(C≡N)R<sup>4</sup>, in which R<sup>4</sup> is hydrogen or alkyl.

4. A compound of claim 3 in which R is methyl, and R<sup>1</sup> is hydrogen.

15 5. The compound of claim 4 in which X is chloro, Y is fluoro, and R<sup>2</sup>  
is (2-cyanoethyl)(methyl)amino.

6. The compound of claim 4 in which X is chloro, Y is fluoro, and R<sup>2</sup>  
is 2-phenoxyethyl.

20 7. The compound of claim 4 in which X is chloro, Y is fluoro, and R<sup>2</sup>  
is 2-cyanopropyl.

8. The compound of claim 4 in which X is chloro, Y is fluoro, and R<sup>2</sup>  
is (methoxy)(methyl)aminocarbonylmethyl.

9. The compound of claim 4 in which X is chloro, Y is fluoro, and R<sup>4</sup>  
is methyl.

25 10. The compound of claim 4 in which X is bromo, Y is fluoro, and R<sup>4</sup>  
is methyl.

11. A compound of claim 3 in which R is methyl, and R<sup>1</sup> is  
acetoxyacetyl.

30 12. The compound of claim 11 in which X is chloro, Y is fluoro, and  
R<sup>2</sup> is dimethylamino.

13. The compound of claim 11 in which X is chloro, Y is fluoro, and R<sup>2</sup> is (2-cyanoethyl)(methyl)amino.

14. A compound of claim 3 in which R is amino, and R<sup>1</sup> is hydrogen.

15. The compound of claim 14 in which X is chloro, Y is hydrogen, and R<sup>2</sup> is 1-cyanoethyl.

16. The compound of claim 14 in which X is chloro, Y is fluoro, and R<sup>2</sup> is 1-cyanoethyl.

17. The compound of claim 14 in which X is chloro, Y is fluoro, and R<sup>2</sup> is dimethylamino.

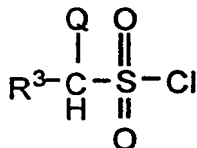
18. A compound of claim 3 in which R is methyl, and R<sup>1</sup> is acetyl.

19. The compound of claim 18 in which X is chloro, Y is fluoro, R<sup>2</sup> is —CH(C≡N)R<sup>4</sup>, and R<sup>4</sup> is methyl.

20. A herbicidal composition comprising an herbicidally effective amount of a compound of claim 1 in admixture with at least one agriculturally acceptable carrier.

21. The method of controlling undesired plant growth which comprises applying to the locus where control is desired a herbicidally effective amount of a composition of claim 20.

22. A compound of the formula



in which :

R<sup>3</sup> is selected from arylhaloalkyl, substituted or disubstituted aminocarbonyl, arylalkoxycarbonylalkyl, and (arylalkylthio)carbonyl; and

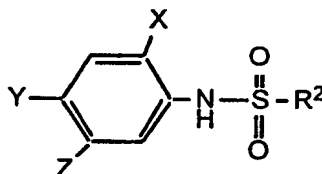
Q is hydrogen or alkyl;

with the proviso that the amino substituents are independently selected from alkyl, cyanoalkyl, alkoxy, alkoxycarbonylalkyl, aryl, arylalkyl, and aryloxyalkyl; the alkyl, alkoxy, and acyl moieties may each contain 1-6

carbon atoms, each may be straight or branched, and the total number of carbon atoms in  $R^3$  does not exceed 12; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with chlorine, bromine, or fluorine.

23. A compound of the formula

5



in which:

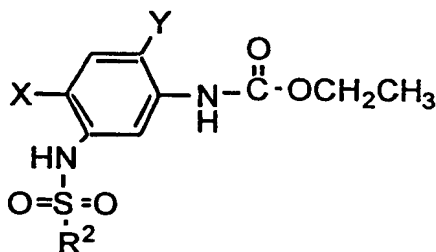
X and Y are independently selected from hydrogen, halogen, and alkyl;

10 Z is nitro, amino, or isocyanato;

$R^2$  is arylalkyl, aryloxyalkyl, cyanoalkyl, substituted or disubstituted aminocarbonylalkyl, arylalkoxycarbonylalkyl, (arylalkylthio)carbonylalkyl, or mono- or disubstituted amino;

with the proviso that the amino substituents are independently  
 15 selected from alkyl, cyanoalkyl, alkoxy, alkoxycarbonylalkyl, acyloxyacyl, aryl, arylalkyl, and aryloxyalkyl; the alkyl, alkoxy, and acyl moieties may each contain 1-6 carbon atoms, each may be straight or branched, and the total number of carbon atoms in  $R^2$  does not exceed 12; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with chlorine,  
 20 bromine, or fluorine.

24. A compound of the formula

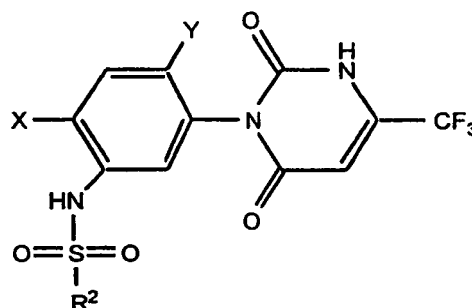


in which:

X and Y are independently selected from hydrogen, halogen and alkyl;  
 $R^2$  is arylalkyl, aryloxyalkyl, cyanoalkyl, substituted or disubstituted  
 aminocarbonylalkyl, arylalkoxycarbonylalkyl, (arylalkylthio)carbonylalkyl, or  
 5 disubstituted amino;

with the proviso that the amino substituents are independently  
 selected from alkyl, cyanoalkyl, alkoxy, alkoxycarbonylalkyl, acyloxyacyl, aryl,  
 arylalkyl, and aryloxyalkyl; the alkyl, alkoxy, and acyl moieties may each  
 contain 1-6 carbon atoms, each may be straight or branched, and the total  
 10 number of carbon atoms in  $R^2$  is does not exceed -12; aryl is selected from  
 phenyl, furanyl, and thienyl, each optionally substituted with chlorine,  
 bromine, or fluorine.

25. A compound of the formula



15

in which:

X and Y are independently selected from hydrogen, halogen, or alkyl;  
 and

$R^2$  is arylalkyl, aryloxyalkyl, cyanoalkyl, substituted or disubstituted  
 20 aminocarbonylalkyl, arylalkoxycarbonylalkyl, (arylalkylthio)carbonylalkyl, or  
 mono- or disubstituted amino,

with the proviso that the amino substituents are independently  
 selected from alkyl, cyanoalkyl, alkoxy, alkoxycarbonylalkyl, acyloxyacyl, aryl,  
 arylalkyl, and aryloxyalkyl; the alkyl, alkoxy, and acyl moieties may each  
 25 contain 1-6 carbon atoms, each may be straight or branched, and the total

number of carbon atoms in  $R^2$  does not exceed 12; aryl is selected from phenyl, furanyl, and thienyl, each optionally substituted with chlorine, bromine, or fluorine.

# INTERNATIONAL SEARCH REPORT

onal Application No

PCT/US 97/23546

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D239/54 C07D405/12 C07C309/81 C07C327/22 A01N43/54

According to International Patent Classification(IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D C07C A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 496 595 A (NISSAN) 29 July 1992 see the whole document ---	1, 20, 23-25
X	EP 0 563 384 A (NISSAN) 6 October 1993 see claims; figures D13,14,92; examples 14,15; table 1 ---	1, 20, 21
X	EP 0 408 382 A (NISSAN) 16 January 1991 see page 89 - page 92; claims; table 3C ---	1, 20, 21
X	WO 94 04511 A (NISSAN) 21 August 1992 see page 1 - page 21 ---	1, 20, 21
X	DE 195 16 785 A (BAYER) 14 November 1996 see claims ---	1, 20
	--- -/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

24 April 1998

Date of mailing of the international search report

08/05/1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Francois, J

# INTERNATIONAL SEARCH REPORT

Inte: Application No

PCT/US 97/23546

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>CHEMICAL ABSTRACTS, vol. 114, no. 4, 1991 Columbus, Ohio, US; abstract no. 223297a, TSUCHIYA, T. ET AL.: "embryo lethality of new herbicides" page 291; XP002063367 see abstract &amp; ARCH. TOXICOL., vol. 65, no. 2, 1991, ENGL., pages 145-148,</p>	1, 20, 21

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Original Application No

PCT/US 97/23546

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 496595 A	29-07-92	AT 127449 T DE 69204480 D DE 69204480 T JP 5004959 A US 5416236 A	15-09-95 12-10-95 02-05-96 14-01-93 16-05-95
EP 563384 A	06-10-93	AU 9070691 A WO 9211244 A JP 5186436 A US 5356863 A	22-07-92 09-07-92 27-07-93 18-10-94
EP 408382 A	16-01-91	AT 143017 T AU 627906 B AU 5884990 A CA 2021005 A DE 69028582 D DE 69028582 T ES 2091799 T US 5084084 A US 5127935 A US 5154755 A JP 3204865 A	15-10-96 03-09-92 17-01-91 15-01-91 24-10-96 10-04-97 16-11-96 28-01-92 07-07-92 13-10-92 06-09-91
WO 9404511 A	03-03-94	AU 2448292 A	15-03-94
DE 19516785 A	14-11-96	AU 5761296 A WO 9635679 A EP 0827497 A	29-11-96 14-11-96 11-03-98